

Substituent effects in thiophenes with particular regard to 3-substituted compounds

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With 3 figures in the text

Introduction

Through the discovery of the commercial thiophene synthesis from butane and sulphur in 1946 (19) new interest in thiophene research grew rapidly, but for 30 years until 1941 it had been carried out mainly by Steinkopf and coworkers (20).

New reactions, more or less specific for thiophene, such as the chloromethylation (21), the formylation with N,N-substituted formamides (22), the metalation with *n*-butyllithium (23), the acylation (24) and alkylation (25) catalyzed by strong oxyacids, to mention some, were discovered.

The main interest of thiophene research, however, has been on the pharmacological plane. Blicke (26), Buu-Hoi (27) and Cymerman-Craig (28), among others, have prepared thiophene analogs of known biologically active benzene derivatives. Their work has almost exclusively been devoted to the easily prepared 2-substituted derivatives.

In recent years thiophene compounds have become of great preparative importance for the synthesis of aliphatic compounds through Raney-nickel desulphurization. Hansen, Buu-Hoi *et al.* and especially Goldfarb and coworkers have shown that aliphatic carboxylic acids (29), amino acids (30), amines (31), alcohols (32), aminoalcohols (33) and ethers (34), can be prepared from thiophene compounds. Fredga (35) has demonstrated the usefulness of Raney-nickel desulphurization of thiophenes for steric correlation of benzene derivatives with aliphatic compounds.

It was soon realized that thiophene showed a very versatile reaction pattern and that superficial statements, which can be found in almost every text-book of organic chemistry, like "thiophene is very similar to benzene, perhaps somewhat more reactive" have only hindered the development of our knowledge of thiophene chemistry. It is ironic that this overemphasis of the similarity between benzene and thiophene stems directly from the discoverer of thiophene, the great Victor Meyer (36). This is understandable, considering the well-known circumstances of its discovery, but it is unfortunate that quantum chemists have a tendency to overestimate the similarity between thiophene and benzene (37). However, in more recent quantum-mechanical calculations (38, 39) the great differences between benzene and thiophene are also stressed. According to Hartough (40) thiophene and benzene ought to be compared "about as closely as a zoologist would compare the tortoise and the boa constrictor, they are in the same class but of widely separated species".

In order to study the aromatic character of thiophene, Fredga and coworkers (41, 42) have investigated optically active 2-substituted thiophenes. As a link in these investigations and in order to elucidate the differences between 2- and 3-substituted thiophenes and the corresponding benzenes, the present author has studied IR- (10), UV- (11) and NMR-spectra (12) of 3-substituted thiophenes, the optical activity of such compounds (13, 14, 16, 17) as well as the directing effect of substituents in position 3 on substitution reactions (6, 7, 9).

Preparation of 3-substituted thiophenes

The first problem connected with this investigation has been to work out methods for the preparation of 3-substituted thiophenes. Since the fundamental work of Victor Meyer it has been known that most substitution occurs almost exclusively in the 2-position. Among the few reactions which are known to lead to predominant 3-substitution may be mentioned the phenylation of thiophene through decomposition of nitroso acetanilide in thiophene (43) and the gas-phase bromination of thiophene (44), discovered some years ago, which gives 3-bromothiophene in low yield. None of these methods are of preparative value. More important however is the sulphuric acid catalyzed alkylation of thiophenes which gives 2- and 3-substitution in about equal amounts (45).

Indirect and tedious methods have therefore been used and only a few compounds have been prepared. The slight knowledge we have had of 3-substituted thiophenes is perhaps best illustrated by the fact that in Hartough's monograph on thiophene, only 8 pages (46) of over 500 are devoted to the 3-substituted compounds.

Since 1948 Campaigne *et al.* (47) have prepared 3-substituted thiophenes from 3-methylthiophene through side-chain bromination with N-bromosuccinimide. The main interest of Campaigne has been to prepare pharmacologically active 3-substituted compounds (48) and to compare their activity with the 2-isomers and the benzene analogs.

The pro and contra of this method has been discussed by the present author (1), and a modification which gives more reproducible results has been introduced. 2-Bromo-3-methylthiophene, which was formed as a by-product in the bromination, could also be utilized for the preparation of 3-substituted thiophenes (2). After completed reaction, the halogen atom was removed through reduction with sodium amalgam. Through these methods, 3-thenylsuccinic acid (1, 2) has been prepared for a study of its optical antipodes.

Because of the difficult availability and high price of 3-methylthiophene, the present author has also studied the chloromethylation of 2,5-dihalogen substituted thiophenes (2). 3-Chlormethyl-2,5-dichlorothiophene was obtained through chloromethylation of 2,5-dichlorothiophene with chloromethyl ether. Via this compound, 3-thenylsuccinic acid was obtained after removal of the chlorine with sodium amalgam.

Most of the 3-substituted thiophenes were prepared from 3-bromothiophene. This compound was synthesized by a method first described by Steinkopf *et al.* (49) who obtained such a low yield that he abandoned this method and worked out another much more tedious route to 3-bromothiophene (50). The present author (3), however, obtained good yield with the first mentioned method which consists in grignardation of both α -bromines of 2,3,5-tribromothiophene in the presence of large amounts of ethyl bromide (entrainment method). Upon hydrolysis of the Grignard compounds

3-bromothiophene was obtained in good yield. As this preparation is the foundation for the subsequent synthesis of 3-substituted thiophenes, the mechanism of the entrainment Grignard reaction has been studied to a certain extent (4).

It has recently been proposed (51) that it should be more suitable and better to carry out the dehalogenation with *n*-butyllithium. It seems however to the present author very improbable that this two-step method which demands the prior preparation of *n*-butyllithium, the preparation and handling of which in large amounts is rather elaborate, can offer any advantage over the one-step entrainment method. The present author (2, 5) however has earlier pointed out that dehalogenation with *n*-butyllithium is of importance in such cases when the entrainment method cannot be used, as in the preparation of 4-bromo-2-thiophenecarboxylic acid from 4,5-dibromo-2-thiophenecarboxylic acid. Recently Imoto *et al.* (52) have described a modification of Steinkopf's second method. They obtained 3-bromothiophene in one step from 4,5-dibromo-2-thiophenecarboxylic acid through simultaneous decarboxylation and debromination with copper powder in quinoline.

From 3-bromothiophene it was possible to obtain 3-methoxythiophene (6) through the cupric oxide catalyzed reaction with sodium methylate in methanol. Most of the 3-substituted thiophenes were however prepared via 3-thienyllithium, which was obtained through halogen-metal interconversion between 3-bromothiophene and *n*-butyllithium (7). Because of the presence of the reactive α -hydrogens, 3-thienyllithium is only stable at low temperature, so the reactions were carried out at -70°C . If the halogen-metal interconversion is carried out at higher temperature, metalation of 3-bromothiophene in the 2-position is obtained. It has been shown by the present author that this is mainly because the initially formed 3-thienyllithium metalates 3-bromothiophene faster than the latter undergoes halogen-metal interconversion with *n*-butyllithium. Similar results have afterwards been obtained by Lawesson in the reaction of 3,4-dibromothiophene (53) and 2,4-dibromothiophene (54) with *n*-butyllithium.

Through the reaction of 3-thienyllithium with carbon dioxide, a convenient method for the preparation of 3-thiophenecarboxylic acid (7) was obtained. 3-Thiophenecarboxaldehyde and 2-(3-thienyl)-ethanol were obtained through the reaction of 3-thienyllithium with *N,N*-dimethylformamide and ethylene oxide respectively (2). 3-Thienylsubstituted secondary alcohols were obtained through the reaction of 3-thienyllithium and aromatic or aliphatic aldehydes (8). These alcohols could easily be oxidized to the corresponding ketones with chromic oxide in acetic acid. Through the reaction of 3-thienyllithium with cyclohexanone and aromatization of the obtained cyclohexenylthiophene, 3-phenylthiophene was prepared in good yield (55). Dimethyl disulphide reacted with 3-thienyllithium to give methyl 3-thienyl sulphide in good yield (9). This compound was easily oxidized with hydrogen peroxide to the corresponding sulphone (9). 3-Thienylsulphinic acid was obtained in the reaction between 3-thienyllithium and sulphur dioxide (9). 3-Thiopheneboronic acid was obtained by Lawesson (56) through the reaction of 3-thienyllithium and *n*-butyl borate.

As 3-thienyllithium is a very reactive and rather unselective reagent, the present author has investigated the possibility of transferring 3-thienyllithium into more selective metal-organic compounds through the reaction with zinc chloride, cadmium chloride and magnesium bromide (8). Through reaction with magnesium bromide, the Grignard reagent free from entrainment Grignard reagent was obtained and through reaction with acetic anhydride at low temperature, 3-acetothienone was

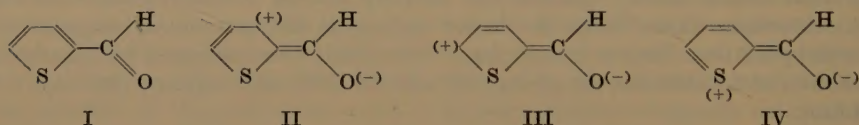
obtained in high yield (8). 3-Thienyllithium reacted slowly with cadmium chloride, but could rapidly be transferred to the zinc organic compound with zinc chloride. In the reaction with acetyl chloride the present author (8, 57) discovered a new type of rearrangement reaction which led to a mixture of 2- and 3-acetothienone. This rearrangement is not specific for the thiophene series but has afterwards independently been found in the benzene series. Thus Klemm, Mann and Lind (58) obtained in the reaction between *meta* methoxybenzenemagnesium bromide, cadmium chloride and *meta* methoxybenzoyl chloride a mixture of the *meta* and *para* isomers.

A new method for the preparation of 3-substituted thiophenes has recently been introduced by Wynberg *et al.* (59). They reacted 3-ketotetrahydrothiophene with Grignard reagents or organolithium compounds. The tertiary alcohols thus obtained were dehydrated and the unsaturated compounds aromatized with chloranil or sulphur. This method however does not offer any advantage over the 3-thienyllithium method for instance for the preparation of 3-phenylthiophene (55).

Through a combination of both methods it should however be possible to prepare otherwise difficultly available compounds. Thus 3,3-dithienyl ought to be easily prepared through the reaction of 3-thienyllithium with 3-ketotetrahydrothiophene.

Effects of substituents in position 2 in thiophene

If the following resonance structures are assumed to contribute to the structure of 2-substituted thiophenes containing a $-I-M$ substituent,¹



it is apparent that the substituent effect is parallel to that in the corresponding benzenes. Structure IV can according to Melander (39) be assumed to have a low mixing coefficient as it contains a $C=S$ double bond. Dipole moment measurements on 2-nitrothiophene (60, 61) and 2-acetothienone (62) are in accordance with this structure. The 3-, 4- and 5-positions can thus with a certain right be compared with the *ortho*, *meta* and *para* positions in substituted benzenes. Until Rinkes' (63) investigations in the earlier 1930's on the nitration of 2-thiophenecarboxylic acid it was also generally believed that electrophilic substitution occurred in the 4-(*meta*-)position. Rinkes however showed that the main product in his nitration experiment was 5-nitro-2-thiophenecarboxylic acid and that thus the place of substitution was determined in competition between the *meta*-directing effect of the substituent and the 5-directing effect of the heterocyclic sulphur. Through different investigations it was soon clear that the proportion of 4- and 5-isomer formed was related to the *meta*-directing strength of the substituent. Steinkopf and Höpner (64) thus found that in the nitration of 2-nitrothiophene, 80 % 2,4-dinitrothiophene, and 20 % 2,5-dinitrothiophene was formed and that in the nitration of 2-thiophene sulphonyl chloride, 75 % of the 4-isomer and 25 % of the 5-isomer was formed. Recently Blatt *et al.* (65) have reinvestigated the nitration of 2-nitrothiophene and obtained about 85 % 2,4-

¹ The terminology of Ingold will be used throughout this paper.

and 15 % 2,5-dinitrothiophene. Blatt points this out especially since some confusion has arisen out of misinterpretation (66) of Steinkopf's results. Recently Tirouflet and Fournari (67) have published some elegant work on the nitration of 2-substituted thiophenes containing a $-I-M$ substituent. The analyses were carried out through polarography. Their results are given in the following table.

	CHO	COCH ₃	CN	COOH	CH(OCOCH ₃) ₂
% 4-isomer	75	52	43	31	14

It is thus apparent that the proportion of 4-isomer rises with increasing *meta*-directing effect of the substituents in the corresponding benzenes, as measured in the ratio *meta* to *ortho-para* or proportion *meta*, when a $-CH_2-$ is included between the phenyl ring and the substituent (68). The effect of a $-I-M$ substituent in the 2-position of thiophene has been discussed at some length as there have lately been tendencies in the literature (56, 69) to overestimate the α -directing effect of the sulphur. The similarity between the 2,5-positions in thiophene and the *para* positions in benzene is also evident from the results of Imoto *et al.* (70). In a study on the esterification and hydrolysis of 5-substituted 2-thiophenecarboxylic acids, they found that Hammett's law was applicable to these compounds and obtained ρ -values which were approximately equal for benzenes and thiophenes.

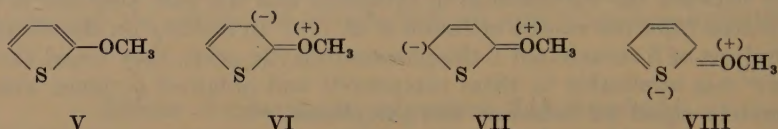
The substituent effect of 2-substituted thiophenes differs noticeably however from the corresponding benzene compounds in certain aspects. Although the classification of substituents has to a large extent been founded on the nitration reaction (71) it is generally believed that the same directing rules also apply to other electrophilic substitutions, at least when the *meta/para* ratio is considered. The present author (5) has pointed out that this seemed not to be the case in the thiophene series. In the bromination of 2-thiophenecarboxaldehyde 5-bromo-2-thiophenecarboxaldehyde was obtained almost exclusively (5); in the corresponding nitration, 75 % of the 4-isomer is obtained (67). The same results have recently been obtained by Buu-Hoi and Lavit (69) apparently independently. It seems improbable that the primary step in the bromination is an addition, as Lawesson (51) did not obtain any addition products in his investigation on the bromination of thiophene. It is of course always possible that the α -bromination occurs via a cyclic mechanism in which the sulphur atom is involved. It should be remembered however that if the *meta* directing group in the 2-position is combined with a $+I$ substituent in position 3, bromination occurs predominantly in the 4-position. Thus according to Steinkopf and Nitschke (72), 4-brom-3-methyl-2-thiophenecarboxylic acid methyl ester is obtained on bromination of 3-methyl 2-thiophenecarboxylic acid methyl ester. The most plausible explanation appears to the present author to be that in the nitration reaction, it is not the effect of for instance the carbonyl group itself which is studied, but of its conjugate acid obtained through the addition of a proton to the carbonyl oxygen of the stronger acidic medium. This neutralizes the negative charge on the oxygen and makes the substituent more effectively *meta*-directing by deactivating the 3- and 5-positions more strongly than the $-C=O$ group itself, the effect of which is measured in the bromination reaction.

Another peculiarity of a $-I-M$ substituent in the 2-position of thiophene as compared with the corresponding benzene derivative is the apparent strong deactivation of the 3-position in thiophene. It is well known from benzene chemistry that the main by-product in electrophilic substitution is the *ortho* isomer (73). In the

corresponding thiophene compound however it is impossible to introduce a substituent in position 3. Thus 2-thiophenecarboxylic acid can only be brominated to the 4,5-dibromo acid (74). Under more vigorous conditions the substituent is eliminated.

When substituents with weak directing effect such as halogens or alkyl groups are introduced in position 2, the strong effect of the sulphur atom dominates, and substitution appears to occur almost exclusively in position 5. The only accurate investigation which has been made is the chlorination of 2-chlorothiophene (75) in which only very minute amounts of the 2,3-isomer were obtained.

If, however, a powerful *ortho-para* directing substituent is introduced in the 2-position, it activates position 3 strongly enough to compete with position 5. Thus Sicé (76) obtained 24 % of 2-methoxy-3-nitrothiophene, and 36 % of 2-methoxy-5-nitrothiophene on nitration of 2-methoxythiophene. This is in accordance with the following structures assumed to contribute to the structure of 2-methoxythiophene (6), from which it can be seen that position 3 and 5 are activated to electrophilic substitution. The 5 position is also activated by the sulphur.



Structure VIII is assumed to be of very low weight, as it has a decet around the sulphur as well as a C=S double bond.

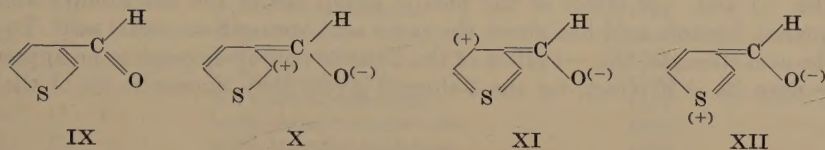
Effects of substituents in position 3 in thiophene

Very little is known about the directing effect of substituents in position 3. 3-Methylthiophene has been investigated to a certain extent. Upon acylation, 20 % of the 5-isomer was obtained (24). In other electrophilic substitutions only minute amounts of this isomer were isolated, and the 2-isomer was obtained almost exclusively (77). Campaigne and Bourgeois (78) have recently investigated the chlorination, bromination and nitration of 3-thiophenecarboxylic acid. They found that the first substituent entered the 5-position and that a second substituent could be introduced into the 2-position, except in nitration where only monosubstitution could be achieved. Campaigne and Monroe (79) have also investigated some substitution reactions of 3-actylaminothiophene and found that monosubstitution occurred in position 2 and disubstitution in positions 2 and 5.

Already Steinkopf (80) observed the ease with which electrophilic substitution occurred in position 4 in thiophenes containing a -I-M substituent in position 3 if the reactive α -positions are blocked with methyl groups or halogens. They managed easily to dinitrate and disulphonate 2,5-dimethylthiophene (49, 81) and 2,5-dibromothiophene (49). Steinkopf (82) also found that three acetoxymercury groups could be introduced in 3-nitrothiophene compared with only two in 2-nitrothiophene under the same conditions. They (49) thus concluded that the 3,4-positions in thiophene could not be compared with either *ortho* or *para* positions in benzene, but reminded one of the *peri* positions in naphthalene if any comparison must be made. The present author and Rosenberg (10) also found that 2,4,5-tribromo-3-thiophenecarboxylic acid could be easily obtained through extensive bromination of 3-thiophenecarboxylic

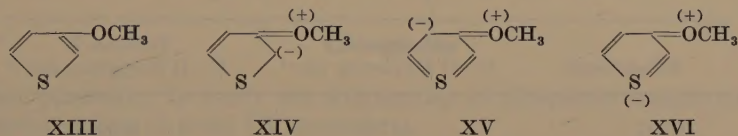
acid. The explanation of Hartough that all these experimental facts can be explained through an addition mechanism seems somewhat unlikely (83).

The present author and Rosenberg (10) suggested, after a discussion of the following resonance structures,



that a structure like XI should have very low weight as it has a decet around the sulphur and that thus a $-I-M$ substituent should not deactivate position 4 in electrophilic substitution in accordance with the experimental results cited above. This is also in accordance with molecular orbital calculations by Melander (39) who also pointed out that structure XII should also have low weight, as it contains a $C=S$ double bond.

The present author (6) has also carried through the corresponding discussions for a $-I+M$ substituent in position 3, exemplified in 3-methoxythiophene. It was suggested that of the following resonance structures, only XIII and XIV are of importance. As a consequence, a $-I+M$ substituent should not conjugatively activate position 4 against electrophilic substitution. Instead, the associated $-I$ effect should deactivate this position.



There are certain experimental results which are in accordance with the suggested structure. As mentioned earlier, a methoxy group in position 2 activates position 3 enough in electrophilic substitution so that this position can compete with position 5, which is also activated by the sulphur (76) towards the reagent. When however an acetylamino group is placed in position 3, monosubstitution is apparently obtained only in position 2 and disubstitution in 2 and 5 (79) although it is known from competitive experiments in the benzene series (84) that the $-NHCOCH_3$ group is a stronger activating *ortho-para* directing substituent than the $-OCH_3$ group.

If we look at the electronic properties of the thienyl nucleus, it seems probable from the suggested structures that the 2-thienyl group is a stronger $+M$ as well as $-M$ substituent than the 3-thienyl group. It should perhaps be pointed out that these conclusions are drawn under the assumption that the quotients of the mixing coefficients for I and II are of the same magnitude as IX and X and in the same manner for V and VI, XIII and XIV, which seems reasonable.

As to the inductive effect, the dissociation constants of 2- and 3-thiophenecarboxylic acid indicate that the electron-attracting inductive effect of the 2-thienyl group is much stronger than that of the 3-thienyl group. 2-Thiophenecarboxylic acid is stronger than the 3-isomer (85), although the conjugation effect should tend to diminish the acid strength more in the 2- than the 3-isomer. (Because of an unfortunate inadvertence it was suggested (10) that the greater acid strength of 2-thiophene-

carboxylic acid was related only to the conjugative effect.) A very extensive discussion of the influence of the inductive and conjugative effects on the acid strength of benzoic acid, and of the possibility to estimate the magnitude of these two opposite effects has been given by Brown *et al.* (86). According to the investigation of Wepster (87), the $-I$ and $+M$ effect of the phenyl group are of the same order and as a consequence, benzoic acid has about the same acid strength as acetic acid. To judge from the acid strength, the $-I$ effect of the 2-thienyl group appears to be appreciably greater than its $+M$ effect, for the 3-thienyl group they appear to be of the same order.

IR-spectra

As a consequence of the suggested structures for 2- and 3-thienylsubstituted carbonyl compounds as the aldehydes and the acids, the $C=O$ bond in 2-substituted compounds ought to have larger single-bond character than in the 3-isomers. A possibility to study the differences in conjugation between these compounds is thus offered by the $C=O$ stretching band in the IR-spectrum (88), as it is generally accepted that conjugation results in a shift of this band towards lower frequency (89, 90 91) and its frequency should be proportional to the force constant, which in turn should be related to the character of the $C=O$ bond. In Table 1, a collection of the $C=O$ frequency for different carbonyl containing 2- and 3-substituted thiophenes is given.

Table 1. $C=O$ frequency of monosubstituted thiophenes.

Substituent	Position 2 $C=O$ frequency cm^{-1}	Position 3 $C=O$ frequency cm^{-1}
CHO	1673	1691
COCH ₃	1658	1674
COCHO · H ₂ O	1673	1689
COOH	1679	1690
COC ₆ H ₅	1636	1652

As can be seen the results are in accordance with stronger conjugation in the 2-isomers. Soloway and Friess (92) have pointed out that there is a connection between the $C=O$ frequency of substituted acetophenones and the carbonyl reactivity as expressed in Hammett's σ -values. They obtained no linear relationship, as some $C=O$ frequencies were measured in the solid state. Later Jolien *et al.* (93) have investigated the $C=O$ frequency of substituted benzophenones in dilute solution and found a linear relationship between $C=O$ frequency, Hammett's σ -values and the half-wave potential in polarographic reduction.

It is therefore of some interest to compare the frequency in the thiophenealdehydes with some substituted benzaldehydes (88) given in the table below.

If the comparison between side-chain reactivity and $C=O$ frequency could be extended to the thiophene series, 2-thiophenealdehyde should undergo carbonyl reactions with a rate comparable with a benzaldehyde heavily substituted with electron-donating substituents such as vanillin and 3-thiophenecarboxaldehyde ought to be comparable with anisic aldehyde. However, few quantitative measurements of such reactions have been carried out. A quantitative study on the rate of alkaline

Table 2. C=O frequency of some aromatic aldehydes.

Aldehyde	C=O frequency, cm ⁻¹
p-Nitrobenzaldehyde	1721
Benzaldehyde	1704
β-Naphthaldehyde	1702
α-Naphthaldehyde	1700
3-Thiophenealdehyde	1691
m-Hydroxybenzaldehyde	1691
p-Hydroxybenzaldehyde	1690
Vanillin	1676
2-Thiophenealdehyde	1673

hydrolysis of the isomeric ethyl thiophenecarboxylates has been carried out by Price *et al.* (85, 94). According to the latest of these investigations it seems that the rates are very similar to that of ethyl benzoate and the order of influence on the rate is 2-thienyl > phenyl > 3-thienyl. This might indicate that a general connection between C=O frequency and reactivity for different series of compounds cannot be expected. This is in accordance with the conclusion of Price (85) that Hammett's σ -values cannot be obtained for thiophene derivatives with benzene as a base. Such σ -values can however be obtained with thiophene as a base which also has been shown by Imoto *et al.* (70) and by Tirouflet and Chané (95).

UV-spectra

Another possibility to study the conjugation in thiophene compounds is offered by an investigation of their UV-spectra.

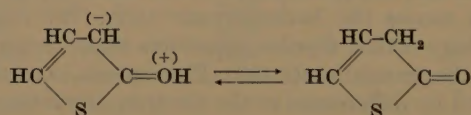
It is well known that increasing conjugation stabilizes the excited state more than the ground state and causes the bathochromic shift. The explanation for this in valence bond terminology is that dipolar structures make larger contributions to the excited state than to the ground state (96). Phenomena involving the excited state should be more affected by differences in the electron-attracting or electron-repelling properties of the substituent than the ground state. There is evidence however that in most cases these effects are similar in the ground state. Thus Doub and Vandenberg (97) found that there was a large parallelity between the bathochromic shift in -I-M substituted benzenes and the -M effect of these substituents. Large parallelity has also been obtained between chemical data for alkyl benzenes and the shifts in their UV-spectra, which led Matsen *et al.* (98) to the conclusion that the excited state produced in aromatic compounds by the absorption of light must resemble in a number of ways the transition state for the substitution reaction.

An investigation of 20 monosubstituted thiophenes (11) has made it possible to interpret the spectra of these compounds to a certain extent and to discuss the difference between 2- and 3-substituted compounds. Larger bathochromic shifts were obtained for 2-substituted thiophenes containing -I-M substituents than for the corresponding 3-isomer, giving additional evidence for the stronger conjugation in the 2-substituted derivatives. Indication for the stronger conjugation in 2-substituted thiophenes containing +M substituents than in the 3-isomers, were also obtained, although in this case the results were not so clear cut.

NMR-spectra

The best possibility for studying the electron distribution at the aromatic hydrogens in the ground state is offered by high resolution nuclear magnetic resonance spectroscopy, since according to Ramsay (99) and Gutowsky *et al.* (100) the chemical shifts observed in proton magnetic resonance due to diamagnetic shielding of the nucleus are connected with differences in the electron distribution around chemical non-equivalent protons. Corio and Dailey (101) have studied monosubstituted benzenes and discussed the connections between the electronic properties of the substituents and the chemical shifts in the NMR-spectra. The situation is, however, more complex with benzene compounds than with the thiophene analogs, since in the former there are five protons, the spin-spin coupling of which complicates the spectra and makes assignment of the protons relatively difficult. In monosubstituted thiophenes on the other hand there are only three aromatic hydrogens and the spin-spin coupling constants can be used for the identification of the different protons (12) in those cases when resolved spectra were obtained. NMR-spectra give the possibility to estimate more quantitatively the difference between the α - and β -hydrogens in thiophene, and facilitate in this way the discussion of the shifts caused through the substituents.

The spectrum of 3-methoxythiophene (12) illustrates the enormous difference between hydrogen 2 and hydrogen 4 giving strong evidence for the correctness of the suggested structure of this compound. The NMR data demonstrate also the permanent nature of the conjugative effect of the methoxyl group. The larger shift for the 3- and 5-hydrogens in 2-methoxythiophene and for the 2 hydrogen in 3-methoxythiophene as compared to the shifts in anisole, make it reasonable that the dipolar structures like VI and VII in 2-methoxythiophene and XIV in 3-methoxythiophene should have larger coefficients than the corresponding resonance structures for anisole. It seems plausible to the present author that there is a connection between the importance of such resonance structures for thiophenes with +M substituents



and the tautomeric nature of the very instable thienols (102, 103). Although no quantitative determination of the equilibrium position of the tautomeric system has been made in solution, the experimental results indicate that the keto form dominates for the 2-isomer. Ford and Mackay (103) state that 3-hydroxythiophene, though also tautomeric, appears to be more phenolic than the 2-isomer.

The NMR-spectra of the isomeric methyl thienyl sulphides indicate that the tautomeric effect of the $-\text{SCH}_3$ group in aromatic substitution is largely electromeric in nature.

The NMR-spectra are also in accordance with the interpretation that a $-\text{I}-\text{M}$ substituent conjugates with the thienyl groups to a greater extent than the phenyl group, although the differences appear to be smaller than when +M substituents are considered. The special effect of the substituent in position 3 on position 4 is also evident (cf. tables in (12)). The connection between the electron-densities obtained from NMR-spectra of $-\text{I}-\text{M}$ substituted compounds and the isomer ratio obtained in electrophilic substitution has been discussed.

Optical activity

Kuhn (104) has recently pointed out that through the large amount of work on the connection between the direction of rotation in optical active compounds and configuration, which arose through the discovery of the Walden inversion, a certain knowledge of the connection between chemical constitution and optical rotation has been obtained, and that through this knowledge optical rotation data should give valuable information about the structure of organic compounds. This was realized 10 years ago by Fredga (41) who started an investigation on optically active thiophene compounds in order to throw some light on the aromatic nature of these compounds. Fredga and his collaborators (105) especially Pettersson (42) have investigated 2-substituted thiophenes, and by extending it to the 3-substituted compounds it was hoped to obtain additional information about the differences and similarities between the phenyl and the 2- and the 3-thienyl nuclei.

The present author has studied 3-thenylsuccinic acid (13) and 3-thienylsuccinic acid (14), the corresponding 2-isomers have been investigated by Fredga and Palm (41) and by Pettersson (106) and the benzene analogs by Fredga (107) and by Pettersson (108). The present author has also investigated both thiophene analogs of mandelic acid (15, 16, 17), as these acids are especially interesting since optically active mandelic acid is a well investigated compound, whose rotation dispersion has been discussed (109).

The first step in the synthesis of 3-thenylsuccinic acid (1) was side-chain bromination of 3-methylthiophene. The 3-thenyl bromide obtained was reacted with triethyl sodium ethane 1,1,2-tricarboxylate and the triester obtained was hydrolyzed and decarboxylated to 3-thenylsuccinic acid. The (−)-antipode was obtained through the strychnine salt and the (+)-antipode through the (+)- α -phenylethylamine salt (13). 3-Thienylsuccinic acid was obtained by condensing 3-thiophenecarboxaldehyde with ethyl malonate adding KCN over the double bond and hydrolyzing and decarboxylating the obtained cyano ester (2). The (+)-antipode was obtained through the cinchonidine salt and the (−)-form through the (−)-phenylethylamine salt (14). The isomeric thienylglycolic acids were obtained through oxidation of the methyl ketones with SeO_2 to the glyoxals and rearrangement of the latter in alkali (15). The (+)-form of the 2-isomer was obtained through the (−)- α -phenylethylamine salt and the (−)-form through the cinchonidine salt (16). The (+)-form of the 3-isomer was obtained through the strychnine salt and the (−)-form through the (+)- α -phenylethylamine salt (17).

The absolute configurations of these acids were determined by the Fredga quasi-racemate method (110) and also through the desulphurization method introduced by Fredga (35). Through this method a new determination of the configuration of mandelic acid has been carried out via 2-thienylglycolic acid (16). The quasi-racemate method has recently been extensively discussed (42, 111). It should therefore only be pointed out that X-ray powder photographs have been used extensively in order to identify the quasi-racemate and they are very useful to correlate thiophene and benzene compounds as the 2- and 3-thienyl compounds often are isomorphous with the benzenes (13, 14). This stresses the view that the large similarity between the thiophenes and benzenes is related to such physical properties as shape, size and molecular weight, which are reflected in the melting and boiling points, and, that these similarities often unfortunately have been generalized to be true for chemical reac-

Table 3. Optical activity of some thienyl and phenyl substituted compounds.

Substituent	[M] _D ²⁵ in ethanol		
	phenyl	2-thienyl	3-thienyl
$\begin{array}{c} \text{H} \\ \\ -\text{C}-\text{COOH} \\ \\ \text{OH} \end{array}$	+ 228° (16)	+ 139° (16)	+ 162° (17)
$\begin{array}{c} \text{H} \\ \\ -\text{C}-\text{COOH} \\ \\ \text{CH}_2\text{COOH} \end{array}$	+ 280° (108)	+ 207° (106)	+ 205° (14)
$\begin{array}{c} \text{H} \\ \\ -\text{CH}_2-\text{C}-\text{COOH} \\ \\ \text{CH}_2\text{COOH} \end{array}$	+ 43.5° (107)	+ 16.3° (41)	+ 32.1° (13)

tivity. The usefulness of the IR-method introduced by Rosenberg and Schotte (112) for the identification of quasi-racemates has also been demonstrated (13, 14, 16, 17).

The rotations in ethanol for the resolved 3-substituted thiophenes and the corresponding 2-isomers and phenyl analogs are given in Table 3.

It can be seen that for the glycolic acids and the acids of the benzylsuccinic acid type the rotation for the 3-isomers lies between those of the phenyl compound and the 2-thienyl derivatives. The rotations of the isomeric thienylsuccinic acids on the other hand show a remarkable similarity in all solvents investigated (14). All these compounds show normal rotation dispersion in the visible which can be represented by the Drude formula. As an example the rotation dispersions for mandelic acid and the thienylglycolic acids are given in Table 4.

Table 4. Rotation dispersions in water.

Compound	[M] ²⁵ in H ₂ O			
	6438	5893	5461	5086
Mandelic acid	+ 189°	+ 229°	+ 277°	+ 337°
3-Thienylglycolic acid	+ 159°	+ 192°	+ 232°	+ 278°
2-Thienylglycolic acid	+ 125°	+ 154°	+ 181°	+ 215°

The experimental material is of course still too small to draw positive conclusions with certainty. However some attempts will be made to discuss the results in terms of the Kuhn-Freudenberg theory on the connection between optical activity and chemical constitution (113).

According to this theory the contribution to the optical rotation from the $250\text{ m}\mu$ band in certain benzenes determines the magnitude of the rotation in the visible region, partly depending upon the fact that this band is near to the visible region, and partly, and what is more important, the vicinal action of the other substituents makes this band highly anisotropic. In order for this benzene band to become anisotropic and the phenyl group thus a dominating (massgebender) substituent it is necessary that the phenyl group is directly attached to the asymmetric center. This is however not enough. In certain cases such as in methyl phenyl carbinol (109) the $250\text{ m}\mu$ band does not become anisotropic and makes no contribution to the rotation in the visible. Rotation dispersion investigations in this band of mandelic acid and hydratropic acid have shown (109) that in these compounds the $250\text{ m}\mu$ band is highly anisotropic. The similar rotation values for phenylsuccinic acid and mandelic acid and their similar dispersion in the visible indicate that this also is the case in phenylsuccinic acid. If in such a dominating substituent small changes are made (e.g. substituents are introduced in the phenyl ring) the contribution to the rotation from this substituent is much changed; the contributions from the other substituents, which in any case are small are changed very little. This offers the possibility for studying the connection between optical activity and the substituent effect in aromatic compounds. Such investigations have been carried out by Betti (114), Rule (115) and Singh *et al.* (116)¹ and their results before 1952 have recently been interpreted in more modern terminology by Nerdel *et al.* (117) who also recently have investigated the connection between optical activity and chemical constitution of the dibenzal compounds of (+)-3-methyl cyclohexanone (118), the benzal compounds of α -phenylethylamine (119) and of substituted hydratropic acids (120). Fredga and Andersson have investigated the isomeric nitro and amino substituted mandelic acids (121, 122, 123).

Pettersson (42) has suggested that the 2-thienyl group is a dominant substituent in those compounds where in the phenyl analog the phenyl group is dominant and that thus the vicinal action of the other substituent is similar on the thiophene analog. This suggestion seems plausible from the similar rotation dispersion in the visible for the phenyl- and thienyl substituted compounds. An investigation of the UV-spectra of thiophenes (11) indicates also that the $235\text{ m}\mu$ chromophore in thiophenes is similar in nature to the $250\text{ m}\mu$ chromophore in benzenes. Pettersson (42) also pointed out that from the material available it is not possible to decide if the lower rotation of the 2-thienyl analogs depends on shorter wavelength of absorption or on smaller anisotropy of the band. A comparison between the isomeric thiophenes is however easier. As can be seen from Figs. 1–3, where the UV-spectra of the optically active thienylglycolic acids, thienylsuccinic acids and thenylsuccinic acids are given, λ_{max} occurs at the same wavelength ($235\text{--}236\text{ m}\mu$) in all isomers. This makes it probable that the different rotations for 2- and 3-substituted compounds are due to differences in the anisotropy of the $235\text{ m}\mu$ band in thiophenes. There might be some connection between the usually greater rotation of 3-substituted compounds and the weaker intensity of their absorption bands, as according to Kuhn (124) weak bands usually have large anisotropy factors.

¹ In this paper reference to earlier works of Singh *et al.* can be found.

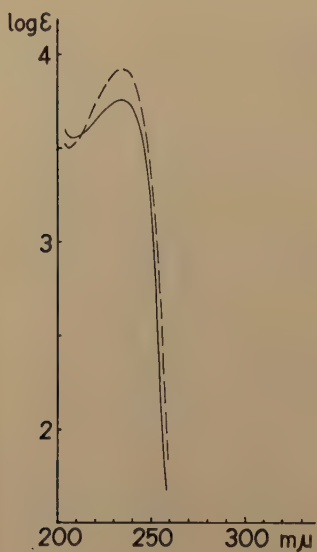


Fig. 1. UV-spectra of ---- (+)-2-thienylsuccinic acid and ——— (+)-3-thienylsuccinic acid.

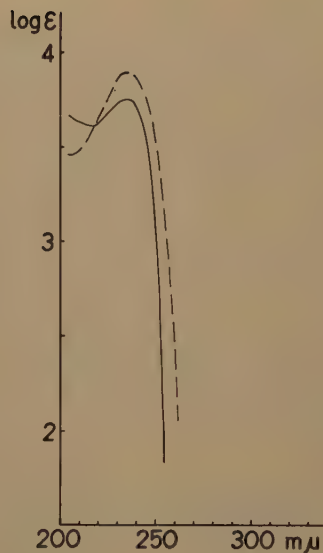


Fig. 2. UV-spectra of ---- (+)-2-thienylsuccinic acid and ——— (+)-3-thienylsuccinic acid.

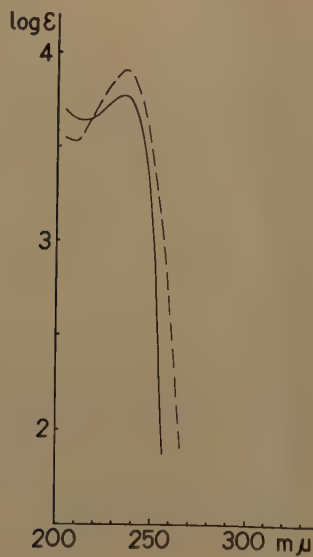


Fig. 3. UV-spectra of ---- (+)-2-thienylglycolic acid and ——— (+)-3-thienylglycolic acid.

Side-chain reactivity in thiophenes

From the physical properties investigated from dipole moment measurements (60-62) and dissociation constants (85) it is apparent that the conjugative electron-attracting $-M$ effect¹ increases in the following series, phenyl < 3-thienyl < 2-thienyl, and that also the conjugative electron repelling effect increases in the same order phenyl < 3-thienyl < 2-thienyl. However especially NMR-data indicate that the difference in $+M$ effect between the phenyl and thienyl groups is smaller than the difference in their $-M$ effect. Finally the inductive effect increases in the same series phenyl $\approx$ 3-thienyl < 2-thienyl. The inductive electron-attracting effect of the 2-thienyl group appears to be much stronger than those of the phenyl and 3-thienyl groups. As mentioned earlier it appears that the $-I$ effects of the phenyl and 3-thienyl groups are of the same magnitude as and opposite in direction to the $+M$ effects, while for the 2-thienyl group $-I > +M$.

With this knowledge of the electronic properties the following predictions about the influence of the thienyl groups on side-chain reactions are possible. The alkaline hydrolysis of aromatic esters, the nucleophilic substitution of benzyl halide type compounds and prototropic reactions of aryl substituted compounds are chosen as examples of different types of side-chain reactions.

It is well known that the alkaline hydrolysis of esters of benzoic acids is retarded by electron donating substituents in the phenyl ring and facilitated by electron-attracting substituents. Thus a $-OCH_3$ group in the *para* position decreases the rate while a nitro group increases the rate of hydrolysis, relative to the unsubstituted esters (125). If we now turn to the thiophene analogs it is evident that the strong $-I$ effect of the 2-thienyl group, strengthened by the inductomeric effect in the same direction, should facilitate the reaction while the $+M$ effects should retard the reaction. As the combined electron-attracting properties are stronger, ethyl 2-thiophenecarboxylate should be hydrolyzed faster than ethyl benzoate. This is in accordance with the latest kinetic measurements of this reaction (94). For the 3-thienyl group the $-I$ effect is of the same magnitude as for phenyl the $+M$ effect is somewhat stronger. Thus ethyl 3-thiophenecarboxylate should be hydrolyzed slower than ethyl benzoate, which also has been found experimentally (85). The characteristic feature of this and analogous reactions should thus be that the rates are of the same magnitude for benzene and thiophene compounds, a little faster in the 2-substituted thiophenes and a little slower in the 3-substituted ones than in the corresponding benzenes.

It is known that nucleophilic aliphatic substitution in benzylhalides is strongly accelerated by conjugatively electron-donating groups such as methoxyl in the *para* position and strongly retarded by electron-attracting groups like $-NO_2$ in the same position. Okamoto and Brown (126) have recently investigated the solvolysis of substituted phenyl dimethyl carbinyl chlorides and found that the *para* methoxy substituted compound reacted 3360 times faster and the *para* nitro compound 3900 times slower than the unsubstituted compound. If we now consider a 2-substituted thiophene, its $-I$ effect should retard the reaction and its $+M$ effect (or better expressed, its associated $+E$ -effect) should facilitate the reaction. It is difficult to decide which effect should dominate. The strong effect of the methoxyl group in benzenes suggests however that the electromeric effect is most important, stabilizing the transition state through extended conjugation with the arising empty p orbital.

¹ For the sake of clarity, note that the electronic characteristics are now being considered from the viewpoint of the aromatic nuclei rather than that of the substituents.

For a 3-substituted thiophene the retarding $-I$ effect is much smaller, but the facilitating $+E$ effect is also smaller than in a 2-substituted compound. Stressing again the importance of the conjugative effects in this type of reactions, it seems plausible that the 2-substituted compound is more reactive than the 3-isomer which in turn reacts faster than the benzene analog. There is some evidence in the literature, at least concerning the reactivity of 2-substituted compounds, which shows that they react faster than the phenyl analogs. Cairns and McKusick (127) and Pettersson (128) found that 2-thenyl chloride in the reaction with sodium cyanide in ethanol gave a mixture of ethyl 2-thenyl ether (25 % yield) and 2-thenyl cyanide (32 % yield) while benzyl chloride under the same conditions gave a high yield of benzyl cyanide uncontaminated with ethyl benzyl ether. Cairns and McKusick (127) also found by allowing benzyl chloride and 2-thenyl chloride to compete for a deficit of sodium amoxide in amyl alcohol that 2-thenyl chloride reacted about three times faster than benzyl chloride.

For the third type of reaction chosen, the effect of the thienyl groups is easily understandable. In prototropic reactions (129) such as the bromination or deuteration of benzylketones or derivatives of phenylacetic acid, or the base catalyzed racemization of the corresponding optically active compounds, the rate-determining step is often the dissociation of a proton from the α -carbon. The effect of substituents in the phenyl group is thus the reverse of the case just discussed. Electron-attracting substituents thus facilitate the ionization of the proton. In this type of reactions, the strong $-I$ effect and $-E$ effect of the 2-thienyl group are in the same direction and the 2-thienyl isomer should undergo such reactions appreciably faster than the phenyl analog. In the 3-isomer, the $-I$ effect is of the same order as in the benzene compound, but its stronger $-E$ effect should render it somewhat more reactive than the benzene compound.

This is in accordance with qualitative observations by Pettersson (106) and by the present author (14) on the base-catalyzed racemization of the isomeric thienylsuccinic acids. Under conditions where phenylsuccinic acid is not racemized at all, partial racemization of 3-thienylsuccinic acid and complete racemization of 2-thienylsuccinic acid is obtained.

In a quantitative study of the base-catalyzed racemization of the phenyl and thienyl substituted glycolic acids at 90° , the present author (17) found that 2-thienylglycolic acid is racemized 33 times faster than mandelic acid and 20 times faster than 3-thienylglycolic acid, in agreement with the predictions made.

Metalation of 3-substituted thiophenes

With the now easy availability of 3-substituted thiophenes and with an increased knowledge of the effect of substituents in position 3, it was of interest to study the effect of substituents on reactions of thiophene. The metalation with *n*-butyllithium has been chosen, as this reaction clearly illustrates differences between thiophene and benzene.

Benzene is metalated extremely slowly and to a very small extent by *n*-butyllithium in ether (130). Most benzene derivatives containing substituents with unshared electron pairs also undergo metalation sluggishly (131). Reaction times of 40–60 hours are normal and the yields are low. Thiophene on the contrary is metalated rapidly and almost quantitatively by *n*-butyllithium in ether (132). Through a study of the

directing effect of substituents in position 3, valuable information about the mechanism of this reaction should be obtained. If the yields are as high as in the metalation of thiophene itself, the reaction is of great preparative importance, not only for the synthesis of otherwise difficultly available thiophene derivatives, but also for the preparation of aliphatic compounds through Raney-nickel desulphurization.

A discussion of the two different interpretations of the mechanism of the metalation has recently been given by Gilman and Morton (133). According to Roberts and Curtin (134) and Sunthakar and Gilman (135) the rate determining step is a nucleophilic attack of the anion on hydrogen. For this type of reaction, Bryce-Smith (136) has introduced the term protophilic. According to these authors the most positively polarized, most acidic hydrogen is attacked by the anion. Morton (137), on the other hand, has suggested that metalation belongs to electrophilic aromatic substitution with Li^+ as the electrophilic reagent. The present author (7) has suggested that the primary step in the metalation of thiophene is the coordination of the metalating agent to the sulphur followed by an attack by the anion on the most acidic hydrogen. It has also been suggested (6) that this coordination to the sulphur is stronger than to a $-\text{OCH}_3$ group, as Sicé (76) exclusively obtained metalation in position 5 in the metalation of 2-methoxythiophene. The suggestion by Sicé that this should depend upon the radicaloid nature of metalation and that radicaloid reagents contrary to electrophilic ones always prefer the α -positions of thiophene seems somewhat unlikely.

The metalation of 3-methylthiophene (7), 3-phenylthiophene (55), 3-methoxythiophene (6), methyl 3-thienyl sulphide (9) and methyl 3-thienyl sulphone (9) has been investigated. In connection with the synthesis of 3-thienyllithium, metalation of 3-bromothiophene (7) was obtained under certain circumstances. The metalated compounds were isolated in the customary manner as the carboxylic acids through reaction with carbon dioxide. The reactions were in all cases very rapid and the yields high, so that the expectations of the preparative usefulness of this method have been fulfilled.

3-Methylthiophene is metalated in position 5, which, as the present author (7) has pointed out, gives strong support for the protophilic mechanism. Electrophilic aromatic substitution occurs as has been mentioned earlier almost exclusively in position 2 (77).

The inductive effect of the phenyl group is contrary to that of the methyl group and metalation should thus be expected to occur in position 2. It has however been found (55) that a mixture of mainly 3-phenyl-5-thiophenecarboxylic acid and 3-phenyl-2-thiophenecarboxylic acid was obtained on carbonation, which could not be separated through fractional crystallization. It could however be proved that the main product was 3-phenyl-5-thiophenecarboxylic acid as upon desulphurization 4-phenylvaleric acid was obtained as the main product. These results may indicate that the metalation with *n*-butyllithium is sensitive for steric effects. Steric effects have also been supposed by Gilman and Spatz (138) to be responsible for the *meta* metalation of triphenylamine.

Especially interesting is the effect of $-\text{I} + \text{M}$ substituents such as $-\text{OCH}_3$, $-\text{SCH}_3$ and $-\text{Br}$. The information obtained through NMR shows that at least the methoxyl group has a permanent conjugative effect in the ground state, which tends to make hydrogen 2 less acidic than hydrogen 5. In spite of this, 3-methoxythiophene (6) as well as methyl 3-thienyl sulphide (9) are metalated in position 2. As there is no reason to suppose that the mechanism for the metalation of these compounds is different from that for 3-methylthiophene, the most probable explanation is that the inductive elec-

tron-attracting effect of the substituents which during the reaction also is strengthened by the inductomeric effect in the same direction, determines the place of substitution. The great importance of the inductive effect in the metalation of benzene derivatives has been pointed out by Wittig (139), although it should be remembered that in the metalation of benzene derivatives, coordination occurs at the substituent which suppresses its conjugative effect besides making it *ortho* directing.

Metalation of methyl 3-thienyl sulphone (9) occurred in the side-chain, showing that the activating effect of the sulphone group is stronger than that of the aromatic sulphur.

In an investigation by the present author and Halvarsson (18) on the isotope effect in the metalation of thiophene containing tracer amounts of 2-tritiumthiophene, it has been found that protium reacts at least six times faster than tritium in the metalation with *n*-butyllithium, showing that the mechanism is different from bromination and nitration of benzene (140) where no isotope effect has been obtained. The large isotope effect is in accordance with protophilic activity of organolithium compounds and shows that the elimination of the hydrogen is the rate-determining step.

Determination of structure of thiophenes

In connection with the experiments on metalation, the problem of the determination of the structure of the products arose. Reliable methods have also become important for structure determination of naturally occurring thiophenes. Wheland (141) has pointed out that the classic method of isomer number is not even theoretically possible in the thiophene series.

The present author has shown that different physical methods can be used with great certainty for the identification of thiophenes. The $13\ \mu$ band in the IR-spectrum can be used to distinguish 3-substituted thiophenes from the 2-isomers (3, 6, 9, 12). It might also be possible, when enough experimental material is available, to use the C-H bending region for the identification of disubstituted thiophenes as in the benzene series (142). There are also characteristic differences in the UV-spectra (11) which can be used for identification.

The best method for identification is provided by the NMR-spectra. It is of course very easy with such spectra to distinguish a symmetrical substituted compound as 2,5-dinitrothiophene from an unsymmetrical as 2,4-dinitrothiophene as in the first mentioned case only one sharp resonance is obtained. It has however been found (9, 12) that the spin-spin coupling constants between the different remaining aromatic hydrogens in the thiophene nucleus can be used for identification of disubstituted thiophenes. The *J* values obtained are $J_{23} = 5.4 \pm 0.6$ c/s; $J_{34} = 3.8 \pm 0.3$ c/s; $J_{25} = 2.7 \pm 0.4$ c/s; $J_{35} = 1.6 \pm 0.3$ c/s. The coupling constants are thus well separated, making identification easy. The variation in a disubstituted series appears from the compounds hitherto recorded, to be about 10 %. The spin-spin coupling constants have been used for the determination of the structure of the product obtained on metalation of methyl 3-thienyl sulphide (9).

Raney-nickel desulphurization has also been used for structure determination (6) and conditions worked out for avoiding the elimination of certain substituents (16). Finally, also cyclization reactions have been used (6) in order to establish structure.

SUMMARY

New methods for the preparation of 3-substituted thiophenes have been worked out. In 3-thienyllithium a very useful intermediate for the preparation of this type of compounds has been found.

IR-spectra, UV-spectra and NMR-spectra of 3-substituted thiophenes have been studied and compared with the corresponding 2-isomers and phenyl analogs. Valuable information about the structural differences in these compounds was obtained, which made it possible to discuss the difference in the effect of substituents in position 2 and position 3 in thiophene on aromatic substitution reactions. An explanation on the special effect of substituents in position 3 on the reactivity in position 4 has been given.

The influence of the isomeric thienyl groups on side-chain reactivity has also been discussed and compared with the benzene analogs. The base-catalyzed racemization of mandelic acid and the thienylglycolic acids has been investigated as an example of such a type of reaction.

The optical activity of 3-substituted thiophenes has been studied and compared with the corresponding 2-isomers and phenyl analogs. The results obtained indicate that in most cases the rotations are larger for the 3-isomers than the 2-isomers. The differences in rotation values seem mainly to depend upon differences in the anisotropy of the 235 m μ band in the thiophenes. The quasi-racemate method has been used for the determination of the configuration of optically active 3-substituted thiophenes. A new determination of the configuration of mandelic acid has been achieved.

The effect of substituents in position 3 on the metalation with *n*-butyllithium has been investigated, and information about the mechanism of this reaction has been obtained. This reaction is very useful for the preparation of various substituted thiophenes.

The use of UV-spectra, IR-spectra and especially NMR-spectra for the determination of the constitution of substituted thiophenes has been discussed. Chemical methods such as Raney-nickel desulphurization and ring-closure reactions have also been used for such determinations.

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Über die Einwirkung der Vorbehandlung und Transformation auf Adsorptions- und Reaktionsfähigkeit verschiedener Glassorten und SiO_2 -Modifikationen

Von J. ARVID HEDVALL

Mit 16 Figuren im Text

ZUSAMMENFASSUNG

Die schnell und vielseitig wachsende wissenschaftliche und technische Anwendung von Glas machte es notwendig, einen Beitrag zu liefern mit Rücksicht auf solche Adsorptions-, Reaktions- und Kristallisationsvorgänge bei Kontakten zwischen Glas und solchen Gasen, Flüssigkeiten und Feststoffen, welche immer noch unvollständig aufgeklärt sind. Es seien als Beispiele erwähnt die Einwirkung der Kühlatmosfera, besonders im Transformationsintervall, die Adsorptionsaktivität oder Angreifbarkeit von Glasgefässen, die in verschiedenen Atmosphären vorbehandelt oder aufbewahrt wurden und die Veränderungen der Glasoberfläche im Kontakt mit oxydchemischen Stoffen, so wie es bei vielen modernen Bau- oder Apparatkonstruktionen der Fall ist.

In dem vorliegenden Beitrag wurde folgendes gezeigt:

Die Reaktions- und Rekristallisationsfähigkeit der verschiedenen SiO_2 -Modifikationen hängt auch im festen Zustand sehr von der Vorbehandlung oder Aufbewahrung in verschiedenen Atmosphären ab. Die genannten Eigenschaften werden nach Vorbehandlung in N_2 , O_2 , SO_2 erhöht, in SO_3 oder $\text{SO}_2 + \text{O}_2$ erniedrigt.

Ähnliches gilt für Adsorptionsaktivität. Bei Versuchen mit Kapillaren, wo also Rekristallisationseffekte ausgeschlossen sind, wurde nach Vorbehandlung des Glases in verschiedenen Gasen oder im Vakuum eine starke diesbezügliche Einwirkung der Strukturumwandlungsvorgänge im Transformationsintervall nachgewiesen. Nur die im O_2 vorbehandelten Kapillaren zeigten keinen solchen Einfluss.

Reaktionsversuche wurden ausgeführt mit Pulvergemischen aus verschiedenen Glassorten und SrO , CaO und MgO , und die Reaktionen von wasserhaltigen und im Vakuum entwässerten Glaspräparaten wurden miteinander verglichen. In sämtlichen Fällen fanden Reaktionen statt. Die entwässerten Präparate waren ausnahmslos weniger reaktionsfähig als die wasserhaltigen. Besonders bei diesen wurden so grosse Reaktionsbeträge erreicht, dass eine Entglasung stattfand. Es wurde auf die Komplexität der Reaktionsverhältnisse aufmerksam gemacht und auf die Rolle der Oberflächenschichten bei den Reaktionen.

In einigen Fällen, d.h. wo bei den Reaktionen die Glasmasse selbst reagiert und keine Kristallisations- oder andere überlagernde Vorgänge in den Oberflächenschichten störend einwirken, wurde ein deutlicher Einfluss auf die Reaktionsfähigkeit durch die Strukturänderungen im Transformationsintervall nachgewiesen.

Die technische Anwendung von Glas zeigt heute eine sehr schnelle Entwicklung. In viel grösserem Masstab als früher wird es als Baumaterial benutzt. In der Elektrotechnik und Elektronik und für chemisch-technische oder wissenschaftliche Apparatkonstruktionen hat es eine wichtige und in vielen Fällen auch ganz neue Bedeutung. Die Glasfabrikation selbst bietet neue Probleme dar, z. B. hinsichtlich der Beständigkeit des Glases gegen das Wannenmaterial oder des physikalisch-chemischen Verhaltens gegen Feuchtigkeit oder andere atmosphärische Bedingungen während der verschiedenen Stufen der Herstellung der fertigen Ware. Auch die Medizin stellt neue Ansprüche auf Beständigkeit von Glasgefässen.

Glas und keramische Produkte verschiedenster Art sind wohl die ältesten synthetischen Erzeugnisse und sie haben alle das gemeinsam, dass die Fabrikation lange, und zu grossen Teilen immer noch auf unvollständiger moderner Kenntnis sowohl von dem Rohmaterial und dem fertigen Produkt als auch von den chemischen Prozessen während der Herstellung ruht. Glas stellt dabei zum Teil eine Ausnahme dar, weil seine Anwendung in der Optik eine Grundforschung verlangte, die mit der Metallographie nahe verwandt war und etwa gleichzeitig entwickelt wurde, d. h. die diesbezügliche Kenntnis der Einwirkung zugesetzter Stoffe. In einem gewissen Sinne gilt dies auch für die Erzeugung von farbigen Gläsern und Glasuren. Eine andere und wenigstens in chemischer Hinsicht bemerkenswerte Sonderstellung besitzen die Zemente, wo die Art der chemischen Verbindungen viel genauer festgestellt ist als immer noch in Glas- oder keramischen Produkten. Erst in neuester Zeit haben die silikatchemischen Industrien eine Zusammenarbeit mit der Grundforschung auf diesem Gebiet aufgenommen, weil es nicht länger möglich war, die immer wachsenden Ansprüche an Qualität der Gegenstände in reproduzierbarer Weise zu erfüllen wie auch den Forderungen an spezifische mechanische oder physikalisch-chemische Eigenschaften von neuen Produkten zu entsprechen.

Die notwendige Bedingung für solche Zusammenarbeit zwischen Grundforschung und Anwendung bildete teils die Kenntnis von den Faktoren, die auf die Reaktionsfähigkeit fester Stoffe mit anderen festen oder mit flüssigen oder gasförmigen Phasen einwirken und teils die Entwicklung der strukturanalytischen Methoden. Was die silikatchemische Fabrikation anbelangt, kamen dabei selbstverständlich die Verhältnisse in oxydischen Systemen in Frage.

Schon die ersten systematisch aufgelegten Arbeiten auf diesem Gebiet (1) zeigten den ausserordentlich grossen Einfluss auf die Reaktionsfähigkeit von den bei festen Stoffen sehr individuellen Strukturverhältnissen. Es seien z. B. die Einwirkung von Herstellungsart (Erbstrukturen), kristallographischen Umwandlungen, verschiedenen kristallographischen Oberflächen und ihren Strukturen, aufgelösten Gasen und von auch ganz kleinen Verunreinigungen (Gastpartikeln) genannt.

Phänomenologisch und durch Messung der Reaktionsfähigkeit in Systemen fest-fest, fest-flüssig und fest-gasförmig wurden solche Effekte viel früher nachgewiesen als moderne röntgenographische oder Elektroneninterferenzmethoden einen detaillierten Aufschluss über Gitterstrukturen ermöglichten. Als Erklärung der auffallend grossen Reaktivitätsunterschiede z. B. von in verschiedener Weise hergestelltem Fe_2O_3 in Gemischen mit CaO wurden Fehlbastrukturen im Gitter angenommen, ehe es möglich war solche direkt nachzuweisen.

Heute wissen wir, dass idealgebaute Kristalle nur ausnahmsweise und unter besonderen Bedingungen existieren. Ganz grob können die materiellen Baufehler in zwei Gruppen eingeteilt werden: solche, deren Konzentration thermodynamisch geregelt ist und einem Gleichgewichtszustand entsprechen und solche, die nicht gleich-

gewichtsmässig auftreten und daher einen Energieüberschuss des Gitters und in der Regel auch erhöhte Reaktivität hervorrufen. So lange dieselbe Modifikation und Gitterart vorliegt wächst die Konzentration der Gleichgewichtsfehler mit steigender Temperatur kontinuierlich nach einer substanzindividuellen Exponentialfunktion. In ebenfalls individueller, aber meistens noch unbestimmter Weise, wandeln sich die anderen Fehler bei höheren Temperaturen, wegen erleichterter Gitterdiffusion, in Gleichgewichtsfehler um.

Es ist heute bekannt, dass die vielen verschiedenen Fehlerarten, worauf hier nicht näher eingegangen wird, eine ausserordentlich wichtige Rolle spielen, nicht nur physikalisch-chemisch, z. B. bei den katalytischen oder ganz allgemein bei Reaktions- und Adsorptionsprozessen, sondern auch physikalisch z. B. bei Halbleitern, Lumino-phoren und Phosphoren. Solche Phänomene und die Effekte, die sie hervorrufen, gehören bereits zu den am lebhaftesten studierten Problemgruppen. Immer noch bietet aber die direkte Beobachtung solcher Gitterstörungen in den meisten Fällen grosse Schwierigkeiten dar.

Im Zusammenhang mit den unten beschriebenen Experimenten über Glasreaktionen soll bloss folgendes erwähnt werden. In der Literatur findet man nicht selten, dass Diffusionsmessungen in Substanzen mit ungenügender Beschreibung sowohl von ihrer Herstellungsweise als auch von der umgebenden Versuchsum-sphäre ausgeführt wurden. Die erhaltenen Werte der Diffusionskoeffizienten können daher als diesbezügliche Substanzkonstanten nicht betrachtet werden. Ferner findet man bei ähnlichen Messungen Extrapolationen von niedrigeren Mess-temperaturen auf höhere, ohne auf die in vielen Fällen eingetretenen Änderungen

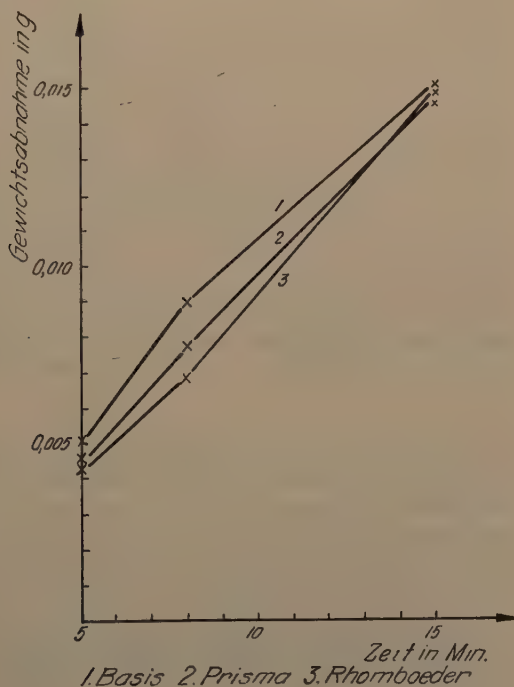


Fig. 1. Der Einfluss verschiedener Kristallflächen auf die Geschwindigkeit des thermischen Zerfalls von CaCO_3 .

des Gittertypus achtzugeben. Ich meine hier nicht Modifikationsänderungen, die diskontinuierliche Änderungen der Diffusionswerte hervorrufen und dadurch auch bestimmt werden können (2), sondern Störungen in Ionengittern in der Form von bei steigender Temperatur wachsenden Konzentrationen von gebildeten molekülähnlichen Atomgruppen. Als Beispiel sei die immer noch mangelhafte Kenntnis des Gitterzustandes beim Erhitzen von CaCO_3 genannt. Die thermische Dissoziations-temperatur liegt bei ca. 900° , wo der CO_2 -Druck also 760 mm beträgt. Weit unterhalb dieser Temperatur können aber beträchtliche Druckwerte gemessen werden, d. h. durch thermische Polarisierung werden CO_2 -ähnliche Gruppen gebildet, die dann in normale Moleküle umgewandelt werden und den Druck erzeugen. Man kann annehmen, dass solche Störungen zuerst an inneren oder äusseren Oberflächen, Kanten und Ecken oder Fehlstellen auftreten, und es war auch zu erwarten, dass diese Vorgänge an kristallographisch verschiedenen Oberflächen mit verschiedener Geschwindigkeit verlaufen (Fig. 1). Vor vielen Jahren (1935) haben wir die Richtigkeit dieser Vermutung experimentell nachgewiesen (3).

Reaktionsversuche mit vorbehandelten SiO_2 -Pulvern

Die erwähnte Einwirkung auf die Reaktivität der benutzten Kristalle auch von nicht reagierenden Gasen, die dabei Gitterstörungen hervorrufen, wurde in verschiedenen Systemen Fest-Gas festgestellt (4).

In diesem Zusammenhang soll folgendes kurz erwähnt werden. Die hier am meisten interessierenden Experimente wurden mit pulverisiertem Quarz, Tridymit, Cristobalit und Quarzglas durchgeführt. Als Vorbehandlungsgase wurden O_2 , N_2 , SO_2 und SO_3 oder SO_2 + Luft angewendet, und die Vorbehandlung der Präparate geschah in dem betreffenden, vollständig trockenen Gase während 2 Stunden in zwei Versuchsreihen bei 600° und 900° . Darauf wurde eine Reihe der Präparate im trockenen N_2 -Strom 1 Stde bei denselben Temperaturen nachbehandelt („gewaschen“) um durch Vergleich mit den „ungewaschenen“ festzustellen, ob die Vorbehandlung bleibende, reaktivitätsändernde Gitterstörungen hervorgerufen hatte. Diese, sowie auch die unter identischen Bedingungen in Luft erhitzten Präparate wurden dann mit durch Erhitzen bei 1000° von CaCO_3 hergestelltem CaO ($\text{CaO}:\text{SiO}_2 = 2:1$) innig gemischt und die Gemische während 1 Stde bei 700 , 800 , 900 und 1000° im trockenen Luftstrom erhitzt. Die nach $2\text{CaO} + \text{SiO}_2 = \text{Ca}_2\text{SiO}_4$ umgesetzte Menge CaO wurde nach der Glykolatmethode bestimmt. Innerhalb der Fehlergrenzen wurde kein eindeutiger Unterschied zwischen den „gewaschenen“ und nicht „gewaschenen“ Präparaten beobachtet.

Tabelle 1.

Reaktions- temperatur	Quarz			Tridymit			Cristobalit			Quarzglas		
	1	2	3	1	2	3	1	2	3	1	2	3
700	5,8	6,3	8,6	—	—	—	—	—	—	6,8	7,3	7,4
800	8,5	10,0	17,6	—	—	—	—	—	—	9,2	10,8	17,4
900	11,5	14,4	25,2	18,2	26,5	45,5	16,7	23,0	37,7	13,3	15,9	19,5
1000	16,0	22,0	37,5	27,7	37,0	33,6	26,7	34,6	29,6	19,7	25,7	30,4

Die Tabelle 1 enthält die Versuchsergebnisse. Die Temperaturen sind in Grad Celsius, und die Zahlen bedeuten die umgesetzten CaO-Mengen in % der Totalmenge CaO. Die Nummern 1 und 2 beziehen sich auf die in Luft und O₂ bei 900° vorbehandelten Präparate. Unter Nr. 3 findet man die Erhöhung der Reaktionsausbeute der „O₂-Präparate“ in % der „Luftpräparate“ (Nr. 1). Die Werte der „N₂-Präparate“ sind nicht mitgenommen; sie unterscheiden sich nicht viel von den „Luftwerten“. In sämtlichen Fällen ist die Aktivierung durch Vorbehandlung grösser bei 900° als bei 600°. Letztere Werte sind in der Tabelle nicht angegeben.

Die Unterschiede des Reaktionsvermögens sind offenbar so gross, dass sie — wie übrigens durch einfache Berechnung feststellbar — nicht *nur* durch Auflockerung der Oberflächenschichten erklärt werden können. Die *relative* Steigerung der Umsetzungsbeträge ist wie zu erwarten für die einzelnen SiO₂-Modifikationen verschieden (Fig. 2). Für Quarz und Quarzglas nimmt sie mit Erhöhung der Reaktionstemperatur zu, für die anderen beiden Modifikationen ab.

Ganz anders liegen die Verhältnisse wenn die SiO₂-Präparate mit SO₃-Gas oder SO₂ + O₂ oder + Luft vorbehandelt und dann wie vorher mit CaO gemischt und reagiert werden. Die Vorbehandlung mit reinem SO₂ zeigt qualitativ denselben aktivierenden Effekt wie mit O₂ und N₂ (in der Tabelle 1 nicht wiedergegeben; man vergleiche die vollständige Veröffentlichung dieser Resultate (5)). Die Tabelle 2 zeigt die Ergebnisse von Vergleichsversuchen für Quarzglas im Luft- und im SO₃-Strom bei 900° vorbehandelt. Die Nummern 1, 2 und 3 beziehen sich auf Luft-, SO₃-Vorbehandlung und prozentuelle *Erniedrigung* im Vergleich zu den „Luftversuchen“ bzw.

Tabelle 2.

Reaktions- temperatur	Quarzglas		
	1	2	3
700	6,8	5,6	17,7
800	8,9	7,3	18,0
900	13,2	9,8	25,9
1000	19,4	13,0	33,0

Es ist in diesem Zusammenhang auch von Interesse zu erwähnen, dass die in verschiedener Weise vorbehandelten Präparate auch in Bezug auf z. B. Methylenblau eine verschiedene *Adsorptionsaktivität* besitzen.

Bei den bis jetzt beschriebenen Versuchen wurde immer mit Pulverpräparaten experimentiert. Wie in einer anderen Arbeit (6) mit Fe₂O₃ als Adsorbens und Reaktionspartner näher nachgewiesen, hängen die Effekte natürlich nicht nur mit Änderungen der Aktivierungsenergie q im Ausdruck $A \cdot e^{-q/RT}$ zusammen sondern auch mit dem oberflächenempfindlichen Faktor A . Das bedeutet, dass auch das Rekristallisationsvermögen und dadurch die Korngrösse beeinflusst wird. Dass andererseits die in den Tabellen beschriebenen Effekte nicht dadurch erklärt werden, geht ohne weiteres daraus hervor, dass die O₂-Versuche einen *erhöhten* und nicht einen durch Oberflächenverminderung *herabgesetzten* Umsatz zeigen. Bei den SO₃-Experi-

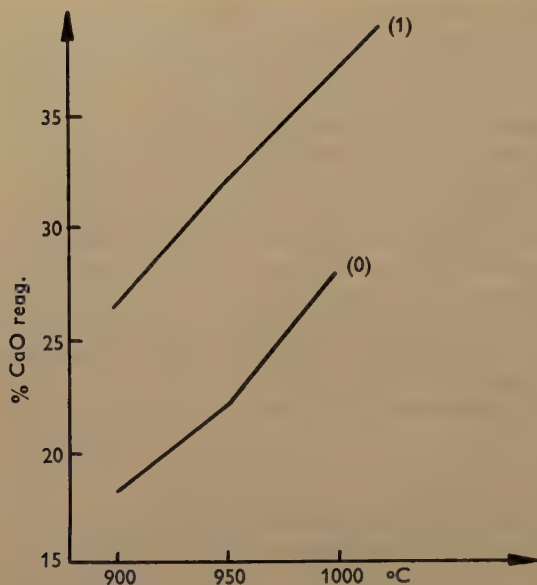


Fig. 2. Umsetzung von im O₂ (1) und in Luft (0) vorbehandelten Tridymit mit CaO.

menten ist es zwar umgekehrt; es wurde allerdings durch Bestimmung der Korngrösse vor und nach der Vorbehandlung nachgewiesen, dass keine der herabgesetzten Umsetzung entsprechende Kornvergrösserung und daraus folgende Oberflächenverminderung eingetreten war.

Es ist jedem Chemiker bekannt, dass die Wärmebehandlung von Röhren oder anderen Glasgeräten durch Aufbewahrung in feuchten Vorratsräumen erschwert oder sogar unmöglich ist wenn sie nicht vorher vorsichtig getrocknet oder entgast werden. Schon BUNSEN (7) stellte fest, dass das Glas die Gase — und besonders H₂O — nicht nur adsorbiert sondern direkt auflöst. Das Interesse an dieser Frage wurde später durch die Vakuumtechnik und die Forderungen an Haushalts- und pharmazeutischen Gefässen stark angeregt, und es wurde festgestellt, dass — wie übrigens selbstverständlich zu erwarten — verschiedene Glassorten sich in dieser Beziehung und in von Struktur und Zusammensetzung abhängiger Weise auch verschieden verhalten. Eine der ersten modernen Arbeiten über die Entgasungsbedingungen aufgelöster Gase wurde von R. G. SHERWOOD (8) ausgeführt. Wir wissen heute wie stark alles dies von den sehr komplizierten und immer noch unvollständig gelösten Strukturfragen der Gläser abhängig ist. Ergebnisse, die mit *einer* Glasqualität oder mit einem unter gegebenen Bedingungen erhitzten und gekühlten Glas erhalten wurden, sind daher nicht unbedingt übertragbar auf andere Gläser oder andere Versuchsbedingungen.

Die Bedingungen der im Folgenden beschriebenen Experimente sind daher so gewählt, dass sie durch Anwendung verschiedener Glassorten, variiert Vorbehandlung (verschiedene Gase oder Vakuum) und verschiedener Versuchstemperaturen, erstens einen Begriff über das Gemeinsame einer gewissen Problemgruppe zu beleuchten versuchen und zweitens, dass sie wenigstens zum Teil den Verhältnissen in der Praxis entsprechen.

Benetzungsversuche

(nach Expp. von S. WALDENSTRÖM u. K. OHLSON)

Über die Struktur vom Glas besteht eine ausserordentlich reiche Literatur (9), eine selbstverständliche Sache, weil die Struktur nicht nur von der Zusammensetzung sondern auch von der thermischen und mechanischen Behandlung abhängt. Aber auch im Falle von in diesen Beziehungen wohldefinierten Produkten — so wie sie hier in Frage kommen — existiert ein grosser Problemkomplex, der heute mit Hilfe moderner Röntgenmethodik eifrig bearbeitet wird. Es ist nicht die Aufgabe der vorliegenden Studien darauf näher einzugehen. Nur das Folgende, rein Prinzipielle soll kurz erwähnt werden.

Schon in den auf diesem Gebiete klassischen Arbeiten von LEBEDEV (10) (1921) wurde die Existenz von kristallinen Keimen der Komponenten oder von im Glas existierenden Verbindungen angenommen und später vielfach röntgenographisch nachgewiesen. PRINS, DEBYE (11) und viele andere Forscher haben den Zustand vom Glas und anderen erstarrten Schmelzen vom thermodynamischen Standpunkt behandelt und stellten fest, dass keine totale Unordnung existiert. Nach PRINS kann der Unterschied zwischen dem kristallisierten und dem flüssigen Zustand als eine Funktion der thermischen Partikeloszillation dargestellt werden. Zu den klassischen Strukturarbeiten, die von denselben und anderen Verfassern modifiziert und weiter entwickelt wurden, gehören natürlich u. a. diejenigen von GOLDSCHMIDT, ZACHARIASEN, WYCKOFF, MOREY, WEYL, ENDELL und DIETZEL (12). Die moderne Entwicklung zum Verständnis der physikalisch-chemischen und mechanischen Eigenschaften vom Glas gründet sich darauf, dass auch die Gläser gitterartig aufgebaut sind und auf durch Strukturbestimmungen ermöglichten Berechnungen der Kräfte der Ionen- oder Molekularbrücken. Es ist allerdings verständlich, dass die erhaltenen Daten kleiner „Bezirke“ des im Ganzen stark ungeordneten Glasgitters nicht in derselben Weise wie bei Kristallen als lokalunabhängige Substanzkonstanten betrachtet werden können. Schon bei chemisch ziemlich einfach zusammengesetzten Kristallen bietet die exakte Berechnung der Einwirkung gewisser Fehlbauarten auf die innere Diffusion oder äussere Reaktionsfähigkeit grosse und noch heute unvollständig beherrschte Schwierigkeiten, und ganz besonders gilt das für die in solchen Zusammenhängen mangelnden Kenntnisse der Oberflächenverhältnisse. Im noch höheren Grad ist dies der Fall bei den in bezug auf Zusammensetzung und Struktur sehr verschiedenen und von der Behandlung stark abhängigen *Gläsern*.

Es ist aus dem angeführten klar, dass es verfrüht und prinzipiell unberechtigt wäre, *Zu detaillierte* Deutungen der in der vorliegenden Arbeit erhaltenen Ergebnisse über Adsorptions- und Reaktionseigenschaften zu versuchen. Das war wie erwähnt natürlich auch nicht die Absicht. Die Versuche und ihre Bedingungen wurden vielmehr so gewählt, dass die Resultate einen Wert besitzen sollten für die verschiedenen Anwendungsgebieten vom Glas. Die Ergebnisse haben aber auch sehr interessante Auskünfte über die rein wissenschaftliche Chemie des Glases gegeben.

Gerade von diesem Gesichtspunkt aus hat es ein besonderes Interesse zu untersuchen, ob die Strukturänderungen im Transformationsintervall einen ähnlichen Einfluss auf das physikalisch-chemische Verhalten der Gläser in bezug auf umgebende, adsorbierte oder reagierende Phasen haben wie die Phasenänderungen in Kristallen.

Die Literatur über Transformationserscheinungen im Glas ist ausserordentlich reich und soll hier nicht näher referiert werden. Hier soll zuerst nur hervorgehoben

werden, dass einerseits die Phasenumwandlung, sowhol in Ionengittern wie auch in solchen organischen Molekülgittern, wo die Vorgänge sich reversibel und bei bestimmten Temperaturen abspielen, und anderseits der Transformationsprozess im Glas keineswegs analog sind. Im letzteren Falle handelt es sich niemals um einen scharfen, substanzindividuellen Umwandlungspunkt sondern um ein sowohl von Erhitzungs- oder Abkühlungsart als auch von der angewandten Bestimmungsmethode mehr oder weniger ausgeprägt abhängiges *Intervall*. FERRY und PARKS (13) haben treffend die Ähnlichkeit zwischen den Änderungen beim Erhitzen vom Glas und von solchen Kunststoffen, wie z.B. Polyäthylene und Polystyrole, hervorgehalten. In beiden Fällen treten Intervalle auf, wo die Verkettungsverhältnisse der aufbauenden Zellen geändert werden und infolgedessen auch die physikalisch-chemischen Eigenschaften. Damit hört allerdings die Analogie dieser Vorgänge auf, weil beim Abkühlen solche Kunststoffe nicht wiederhergestellt werden.

Trotz der wie erwähnt grossen Zahl von diesbezüglichen Untersuchungen (14) ist es bei den verschiedenen und verschieden behandelten Gläsern nicht möglich von vornherein zu beurteilen in welcher Weise die im Transformationsintervall eintretenden Änderungen auf Adsorptionsaktivität oder Reaktivität einwirken. Dies hängt natürlich u.a. mit den Dipoleigenschaften und der Orientierung der Gerüstzellen zusammen. Dass allerdings irgendeine Änderung auch in dieser Beziehung sich im Transformationsintervall bemerkbar machen wird, lässt sich schon aus der Änderung der inneren Energie voraussehen (15).

Wenn im Folgenden trotzdem die „Transformationspunkte“ angegeben werden, so ist im Gedächtnis zu behalten, erstens dass diese Temperaturen als Punkte *innerhalb eines Intervalls* liegen, das mit einer sogenannten *Vorerweichung* beginnt und zweitens, dass die Breite des Intervalls je nach der Substanzart mehr oder weniger von thermischer und mechanischer Behandlung abhängt und dass diese Verhältnisse natürlich auch auf das chemische Verhalten des Glases einwirken.

Um den Einfluss von Änderungen der Oberflächengrösse wegzulassen, wurden Benetzungsmessungen mit in denselben Gasen wie vorher vorbehandelten Glaskapillaren gemacht. Zur Anwendung kam ein Jena-Supremaxglas von der Zusammensetzung:

$\text{SiO}_2 = 58,9 \%$	$\text{TiO}_2 = 0,1 \%$	$\text{MgO} = 9,7 \%$
$\text{Al}_2\text{O}_3 = 23,5$	$\text{CaO} = 5,1$	$\text{K}_2\text{O} = 0,4$
$\text{Fe}_2\text{O}_3 = 0,5$	$\text{BaO} = 0,2$	$\text{Na}_2\text{O} = 1,1$
$\text{B}_2\text{O}_3 = 0,6$		

Die Oberflächenaktivität wurde durch Messung der Steighöhe von vollkommen reinem H_2O bei 20° gemessen und der Benetzungsgrad in $\alpha \cdot \cos \phi$ ausgedrückt.

Vollständig trocken und in üblicher Weise von anderen Gasen befreit wurden N_2 , O_2 , SO_2 und CO_2 als Vorbehandlungsgase angewendet. Bei den SO_3 -Versuchen wurde ein vollständig trockenes, in einem Glasrohr aufbewartes kristallisiertes SO_3 -Präparat benutzt. Die Spitzen des Rohres wurden abgebrochen, ein trockener Strom von N_2 durchgeleitet und das N_2 - SO_3 -Gemisch durch den Ofen, wo die Glaskapillaren bei den verschiedenen Versuchstemperaturen erhitzt wurden, geführt. Danach wurde mit N_2 „gewaschen“ um die wasseranziehende Adsorptionsschicht von SO_3 zu entfernen. Der „Transformationspunkt“ wurde zu ca. 520° bestimmt. Der „Kegelschmelzpunkt“ des Glases, d.h. die Temperatur wo die erhitzten Kapillaren anfangen sich ohne Belastung zu biegen wurde zu 760° bestimmt. Bei höheren Temperaturen findet bei diesem Glas eine sehr langsam verlaufende Deformierung statt.

Diskussion der Messungen

Vakuumvorbehandlung

In Übereinstimmung mit dem Ergebnis von SHERWOOD entweichen bei Temperaturen unter dem „Transformationspunkt“ aufgelöste Gase und die Benetzungsfähigkeit steigt nach Behandlung bei erhöhter Temperatur. Bei noch höheren Behandlungstemperaturen treten Veränderungen in der Glasstruktur auf, die die Benetzungsfähigkeit des angewendeten Glases wieder herabsetzen (Fig. 3) wenn das Glas nicht mit gewissen Gasen behandelt wird. Wenn das evakuierte Glas über die Erweichungstemperatur erhitzt wird nimmt $\alpha \cos \phi$ einen negativen Wert an, und das Wasser steigt wieder in die Kapillaren hinauf erst wenn man es eine Zeit an der Luft liegen lässt.

Gasvorbehandlung

Die N_2 -, CO_2 - und SO_2 -kurven haben alle in grossen Zügen denselben Typus, d.h. der Benetzungsgrad steigt bei wachsender Vorbehandlungstemperatur zu einem relativen Maximum im Gebiet der beginnenden Transformation und fällt wieder nach der mehr oder weniger vollständigen Strukturänderung in diesem Intervall. Bei noch höheren Vorbehandlungstemperaturen steigt der Benetzungsgrad wieder langsam (Fig. 4–7).

Die vorangehende Vacuumbehandlung ändert *im Prinzip* nichts. Es wurde schon in den in diesem Zusammenhang klassischen Arbeiten von SHERWOOD hervorgehalten, dass die Benetzungseffekte von drei Faktoren abhängig sind, nämlich von der Struktur des Glases, von den aufgelösten oder chemisch gebundenen Gasen und von den nur adsorbierten. Da die Probleme der Glasstruktur in vielen und besonders in unserem Zusammenhang wichtigen Teilen unvollständig gelöst sind, kann vorläufig eigentlich nur folgendes angeführt werden: Die Ergebnisse sind, sofern sie mit den SHERWOOD-

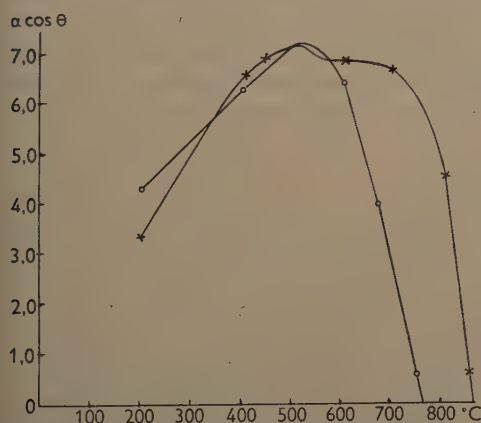


Fig. 3. Benetzbarkeit nach Vorbehandlung der Glaskapillaren im Vakuum 1 Stde (x); 3 Stdn (o).

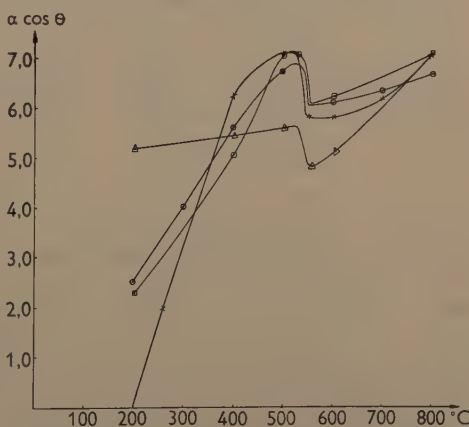


Fig. 4. Benetzbarkeit nach Vorbehandlung der Glaskapillaren im N_2 3 Stdn (x); 5 Stdn (o); Vakuum 1 Stde bei 800°, dann im O_2 2 Stdn und im Exsiccator 1 Stde (Δ); Vakuum 1 Stde bei 800°, dann im O_2 2 Stdn und im Exsiccator 1 Woche ($\square$).

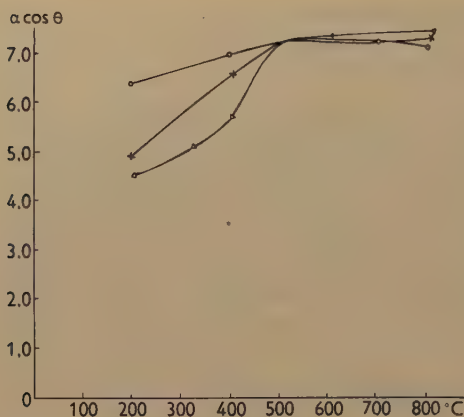


Fig. 5. Benetzbarkeit nach Vorbehandlung der Glaskapillaren im O_2 1 Stde (×); 3 Stdn (○); Vakuum 1 Stde bei 800° , dann im O_2 2 Stdn und im Exsiccator 1 Stde (Δ).

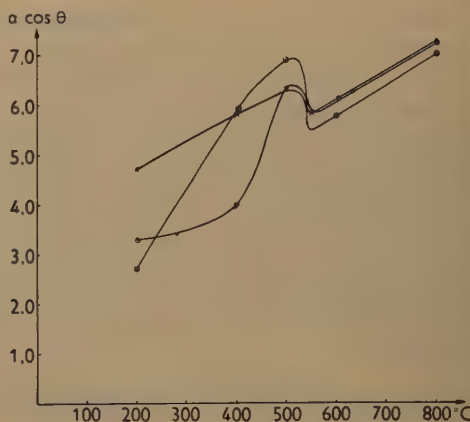


Fig. 6. Benetzbarkeit nach Vorbehandlung der Glaskapillaren im SO_2 1 Stde (×); 3 Stdn (○); Vakuum 1 Stde bei 800° , dann im SO_2 2 Stdn und im Exsiccator 1 Stde (Δ).

schen vergleichbar sind, in guter Übereinstimmung. Bei den Temperaturen über dem Transformationsintervall hat man wohl hauptsächlich mit dem Einfluss von adsorptiv gebundenen Gasen zu rechnen. Es muss aber unterstrichen werden, dass es — und ganz besonders bei amorphen Substanzen — in vielen Zusammenhängen kaum berechtigt ist, scharfe Grenzen zwischen aufgelösten, chemisch gebundenen und adsorbierten Gasmengen zu ziehen. Stöchiometrische Abweichungen im Festkörper kommen dabei auch in Betracht, worauf besonders moderne Arbeiten über die elektrische Leitfähigkeit der Gläser aufmerksam machen.

Dieser Gesichtspunkt liegt nahe mit in Rechnung zu nehmen bei einem Versuch den ganz verschiedenen Verlauf der O_2 -Kurven (Fig. 5) zu erklären. Das Glas ist eine „oxydische“ Substanz und man kann vielleicht vermuten, dass sein Verhalten in Bezug auf Sauerstoff anders ist als gegen andere Gase. Am meisten auffallend ist, dass der Transformationsprozess sich nicht bemerkbar macht (16).

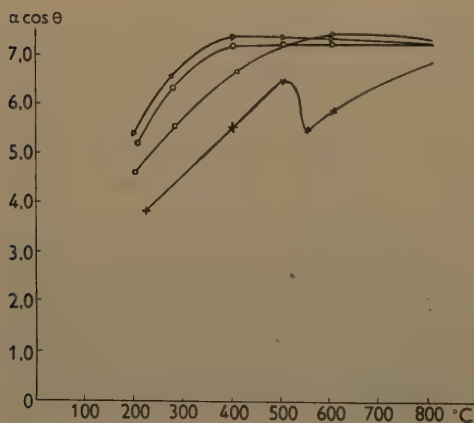


Fig. 7. Benetzbarkeit nach Vorbehandlung der Glaskapillaren im CO_2 3 Stdn (×); SO_3 2 Stdn, N_2 1 Stde (○); Vakuum bei 800° , dann im SO_3 1 Stde, N_2 1 Stde und im Exsiccator 1 Stde (Δ); Vakuum bei 800° 1 Stde, dann im SO_3 1 Stde, N_2 1 Stde und im Exsiccator 1 Woche (□).

Es ist ersichtlich dass die O_2 -Vorbehandlung am meisten aktivierend wirkt was sich auch darin ausdrückt, dass das Wasser viel schneller in die Kapillare aufsteigt als bei der Vorbehandlung mit anderen Gasen.

Die Einwirkung der Vorbehandlung mit SO_3 ist selbstverständlich mit den anderen nicht zu vergleichen, weil SO_3 mit den „basischen“ Oxyden im Glas direkt reagiert. Das Glas wird nach der SO_3 -Behandlung auch spröde. Wenn trotz des „Waschens“ mit N_2 jedoch eine SO_3 -Haut adsorbiert bleibt, wirkt diese natürlich auch stark wasseranziehend (Fig. 7).

Allgemeines über den Reaktionsmechanismus in festen hier interessierenden Substanzen

Einleitend werden einige Ergebnisse von früheren Reaktionsversuchen in Pulvergemischen aus Oxyden und Silikaten genannt. *Direkt* anwendbar im vorliegenden Zusammenhang sind sie zum Teil nicht, weil sowohl die Struktur als auch die Existenz chemischer Verbindungen im Glas anders ist als bei einzelnen kristallisierten Substanzen. Schon heute und noch mehr je nachdem die Forschung unsere Kenntnisse von den Strukturverhältnissen im Glas vertiefen lässt, liefern sie jedoch einen Beitrag auch zur Deutung der Umsetzungsprozesse.

Im folgenden nur eine kurze Zusammenfassung und Literaturhinweise diesbezüglicher Ergebnisse. Es hat einen Wert, eine Zusammenfassung der in vielen Zeitschriften verbreiteten Ergebnisse zu machen:

Unter sonst vergleichbaren Bedingungen (Korngrösse 0,05 mm) wurde wie erwartet nachgewiesen, dass glasiges SiO_2 mit den Oxyden von Mg, Ca, Sr und Ba schneller reagiert als die kristallisierten Modifikationen (17).

Die erste Veröffentlichung (1922) eines vorher unbekannten Reaktionstypus zeigte, dass Pulverumsetzungen nach der Formel:



wo $M'O$ und $M''O$ Oxyde, $M'XO_n$ und $M''XO_n$ Salze von Sauerstoffsäuren sind und Q die Reaktionswärme, *auch* in Gemischen von z. B. MgO oder Erdalkalioxyden mit Silikaten schnell bei verhältnismässig niedrigen und hauptsächlich von dem Zusatzoxyd abhängigen Temperaturen (ca. 550° für CaO und MgO , ca. 450° für SrO und ca. 350° für BaO) verlaufen. (18) In Gemischen mit Silikaten können natürlich auch Doppelsilikate gebildet werden, z. B. nach: $CaO + MSiO_3 = CaMSiO_4$. Der Verlauf der Umsetzung hängt von der Temperatur und Dauer der Versuche ab, d. h. von den Diffusionsgeschwindigkeiten in den Komponenten, bei der Phasengrenze und in den gebildeten Reaktionsprodukten. JANDER hat nachgewiesen, dass auch in Gemischen von CaO und SiO_2 im Verhältnis 1:1 *zuerst* das Orthosilikat gebildet wird (19) (vgl. unten). Aus einer Arbeit vom Verfasser über Reaktionen zwischen CaO und Pb- und Mn-Silikaten sei folgendes zitiert (20): „Bei Reaktionen im festen Zustand in Gemischen aus Kalk in grossem Überschuss und den Metasilikaten von Pb und Mn bilden sich (unter 800°) die Doppelsalze $CaPbSiO_4$ und $CaMnSiO_4$. Mit Pb_2SiO_4 erhält man unter denselben Bedingungen nicht eine additive Umsetzung sondern eine Austauschreaktion nach: $2CaO + Pb_2SiO_4 = Ca_2SiO_4 + 2PbO$ “. Dabei spielt offenbar die bei den erwähnten Versuche von JANDER bevorzugte Bildung von dem Orthosilikat unter den gegebenen Bedingungen die Hauptrolle (vgl. auch unten). R. LINDNER hat in unserem Institut die Selbstdiffusion in CaO mit Hilfe von dem radioaktiven Ca-Isotop bestimmt und dafür den Ausdruck: $D = 0,4 \exp. (-81000/RT) \text{ cm}^2\text{sec}^{-1}$ gefunden (21).

Eine andere Arbeit von LINDNER über die Bildung von Ca- und Pb-Silikaten unter Anwendung von Radioisotopen hat in unserem Zusammenhang ein so grosses Interesse, dass ein ausführlicherer Auszug durchaus berechtigt ist (22).

„Bleisilikate haben grosses Interesse für die Glasindustrie ('Flintglas' hoher Dichte). Auf Grund der grossen Polarisierbarkeit seiner Ionen kann Blei in grosser Menge in Silikatgläsern eingebaut werden (23). Die Verwendung radioaktiver Isotope für in diesem System auftretende Reaktionen ist gegeben, da in Pb-212 (Thorium B) und Pb-210 (Radium D) geeignete Isotope in beliebiger Menge zur Verfügung stehen.

Das System PbO + SiO₂ ist eingehend untersucht worden (24), wobei sich die Existenz folgender Silikate ergab: PbSiO₃ (Fp = 766°C), Pb₂SiO₄ (Fp = 746°C) und Pb₄SiO₆ (Fp = 725°C). Die Eutektika des Systems liegen bei 717°. Pb₄SiO₆ zeigt Umwandlungen bei 720° sowie bei 120° bis 155°, während für Pb₂SiO₄ eine Umwandlung bei 620° angegeben wird und in neuester Zeit auch eine Umwandlung bei PbSiO₃ bei 585° aufgefunden worden ist (25 u. 26).

An verwertbaren Angaben über die *Reaktion im festen Zustand* in diesem System sind die von TAMMANN und KALDING (27) (Reaktionsbeginn laut thermischer Analyse bei 580°C) und von HEDVALL und ELDH (28) zu nennen. Letztere arbeiteten mit reinstem Quarz von definierter Korngrösse und bekannten Erhitzungstemperaturen und -zeiten und erhielten 25 % Umsetzungsgrad nach Erhitzung auf 650° während einer Stunde.

JAGITSCH und BENGTSON (29) ermittelten die Reaktionskonstante für die Bildung von Pb₂SiO₄ und Pb₄SiO₆ durch Reaktion von gesinterten Presstabletten von PbO/PbSiO₃ bzw. PbO/Pb₂SiO₄. Darüber hinaus fanden JAGITSCH und BENGTSON mittels der „Methode der Markierung der ursprünglichen Grenzfläche“ (30), dass sich die Reaktionsschicht ausschliesslich auf der kieselsäurereichen Seite der Systeme aufbaut, woraus der Schluss gezogen wird, dass Transport von Blei und Sauerstoff durch die Reaktionsschicht stattfindet, dagegen kein Transport von Silicium in entgegengesetzter Richtung.

Mittels des Bleiisotopes Pb-212 (Th B) (10,6 Stunden Halbwertszeit) und der Methoden der Absorption von α-Strahlung sowie der „Kontaktmethode“ wurde die Diffusion von Blei in Sinter-tabletten von PbSiO₃ and Pb₂SiO₄ gemessen (25).

Die Temperaturfunktionen der Selbstdiffusionskonstanten liessen sich (abgesehen von relativen Maxima bei 585°C im PbSiO₃ und 620° im Pb₂SiO₄) wiedergeben durch

$$D = 85 \exp (-59500/RT) \text{ cm}^2\text{sec}^{-1} (\text{PbSiO}_3)$$

und

$$D = 0,2 \exp (-47000/RT) \text{ cm}^2\text{sec}^{-1} (\text{Pb}_2\text{SiO}_4).$$

Die Calciumsilikatbildung

Die Bildung der Verbindung zwischen Kalk und Kieselsäure in verschiedenen Mengenverhältnissen gehört zu den am gründlichsten untersuchten Festkörperreaktionen, u. a. wegen der Bedeutung der verschiedenen Kalksilikate für Fragen der Mineralogie und der Zementherstellung.

An klassischen Arbeiten in diesem Gebiet sind zu nennen die von RANKIN (31) (Zustandsdiagramm); HEDVALL (17) (Reaktion zwischen CaO und SiO₂, echte Reaktion im festen Zustand); DYCKERHOFF (32) (Charakterisierung der reinen Calciumsilikate durch ihre optischen Konstanten, Angaben über den Verlauf der Reaktion auf Grund mikroskopischer Untersuchung und thermischer Analyse); WEYER (33) (Bestimmung des Umsatzes durch Röntgendiagramme); HILD und TRÖMEL (34) stellten in Übereinstimmung mit DYCKERHOFF das Orthosilikat als primäres Reaktionsprodukt fest. Zu den gleichen Ergebnissen gelangten auch JANDER und HOFFMANN (19), die mittels genauer Analysenmethoden den Reaktionsverlauf verfolgten. Als wahrscheinliches Bild für den Reaktionsmechanismus ergab sich das folgende: An der Phasengrenze der Ausgangs-

oxyde verläuft die Reaktion bevorzugt zu Orthosilikat, sekundär erfolgt mit geringerer Geschwindigkeit die Bildung kieselsäurereicherer Silikate ($\text{Ca}_3\text{Si}_2\text{O}_7$, bzw. CaSiO_3) in Berührung mit der Kieselsäure, während bei Temperaturen über 1300°C auf der Seite des Calciumoxydes auch die Bildung eines hochbasischen Silikats (Ca_3SiO_5) angenommen wird. Bei äquimolaren Mengen wird das Calciumoxyd vorzeitig infolge der Bildung höherbasischer Verbindungen verbraucht, wonach jedoch die Diffusion aus diesen zur Kieselsäure hin eintritt, bis gleichmässige Verteilung vorliegt, d.h. das Metasilikat sich gebildet hat.

Die Untersuchung dieser Reaktion stellt eine schwierige Aufgabe dar: Nicht nur, dass eine „Simultanreaktion“ mit vier verschiedenen Reaktionsprodukten vorliegt, die wohl nur unter gewissen vereinfachenden Annahmen analysierbar ist; fast alle Reaktionsprodukte weisen bei verschiedenen Temperaturen kristallographische Umwandlungen auf, was erhebliche unetstetige Veränderungen der Beweglichkeitsverhältnisse mit sich führen kann. So liegen z. B. beim Calciumorthosilikat vier verschiedene Modifikationen vor, nämlich die α -Modifikation, beständig zwischen dem Schmelzpunkt und ca. 1400°C , die α' -Modifikation (unterhalb ca. 1400°C), die sich entweder bei 850°C in die γ -Modifikation oder aber bei 675°C in die β -Modifikation umwandelt.

Für das CaSiO_3 wird eine Umwandlung bei 1125°C angenommen, während bei $\text{Ca}_3\text{Si}_2\text{O}_7$ auf Grund der weiter unten besprochenen Selbstdiffusionsmessungen eine Umwandlung bei ca. 1260°C vermutet wird.

Als unumgängliche Vorbedingung eines späteren Versuches der genauen Analyse der Calciumsilikatbildung erschien uns die Messung der Selbstdiffusionskonstanten in den verschiedenen Silikaten.

Bestimmung der Selbstdiffusion von Calcium

Als Indikator wurde ausschliesslich Ca-45 (Halbwertszeit 180 Tage) verwendet.

a) CaSiO_3 , Calciummetasilikat (Wollastonit)

Die Diffusion von Calcium in der Hochtemperaturmodifikation wurde im Bereich von 1130° bis 1400°C gemessen, wobei die Temperaturfunktion: $D = 7 \cdot 10^4 \exp(-112000/RT)$ $\text{cm}^2\text{sec}^{-1}$ erhalten wurde (35). Unterhalb der Umwandlung sind die Messungen infolge der geringeren Diffusionskonstante erheblich schwieriger, und der den bisherigen Werten zuzuordnende Ausdruck: $D = 0,2 \exp(-78000/RT)$ $\text{cm}^2\text{sec}^{-1}$ ist als vorläufig anzusehen. Im α -Wollastonit wurde auch eine erhebliche Ionenleitfähigkeit durch (radioaktive) Überführungsmessungen gefunden, die Überföhrungszahl variiert zwischen 10 und 1 % bei Temperaturen zwischen 1220° und 1130°C . Extrapoliert man die Überföhrungszahlen auf die Schmelztemperatur, so ergibt sich 100%ige Calciumionenleitung, was gut mit dem Befund von Bockris (36) an Silikatschmelzen übereinstimmt. Die annähernde Übereinstimmung der aus der spezifischen Ionenleitfähigkeit berechneten mit den gemessenen Selbstdiffusionskonstanten führt zur Annahme des ausschliesslichen Ionencharakters des diffundierenden Calciums.

b) $\text{Ca}_3\text{Si}_2\text{O}_7$

Hier wurde die Diffusion radioaktiven Calciums von LINDNER und OBERMAYER (37) bei Temperaturen zwischen 1000° und 1400°C gemessen und eine Unstetigkeit im Temperaturverlauf der Diffusionskonstante bei etwa 1260°C gefunden, unterhalb welcher die Temperaturfunktion durch den Ausdruck $D = 10^{-2} \exp(-73000/RT)$ $\text{cm}^2\text{sec}^{-1}$ beschrieben werden kann.

c) Ca_2SiO_4 , Calciumorthosilikat

Wegen der α' - β Umwandlung bei 850°C (die wir bei den von uns hergestellten Sintertabletten im Gegensatz zu den Angaben der Literatur nicht unterdrücken konnten), musste die Radioaktivität des Präparates während der Erhitzung gemessen werden, was mit Hilfe eines spezial-

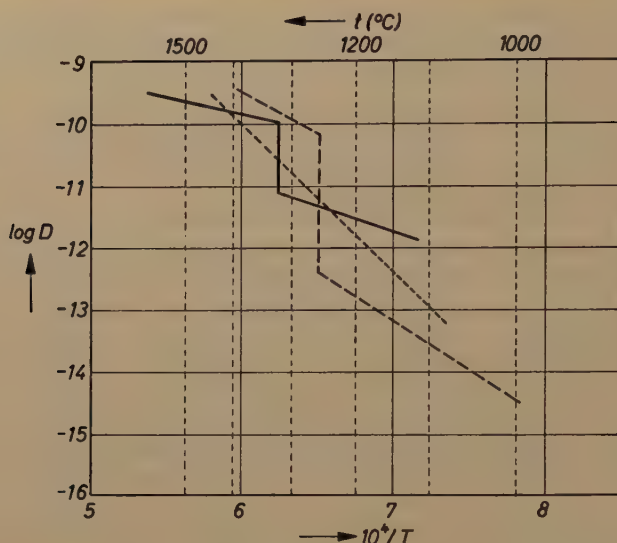


Fig. 8. Temperaturfunktion der Selbstdiffusion von Calcium in Ca_2SiO_4 (ausgezogen), CaSiO_3 (punktirt) und $\text{Ca}_3\text{Si}_2\text{O}_7$ (gestrichelt).

konstruierten Ofens möglich war (38). Die Temperaturfunktion der Selbstdiffusionskonstante zeigte eine Unstetigkeit im Zusammenhang mit der α' - α Umwandlung des Silikates, die entsprechende Temperatur lag allerdings (eventuell wegen Verunreinigung durch Platin) mit 1370°C erheblich tiefer als die Werte der Literatur. Die Temperaturfunktionen werden durch die folgenden Ausdrücke wiedergegeben:

$$\alpha'\text{-Ca}_2\text{SiO}_4: D = 3,6 \cdot 10^{-2} \exp(-65\,000/RT) \text{ cm}^2\text{sec}^{-1}$$

$$\alpha\text{-Ca}_2\text{SiO}_4: D = 2,0 \cdot 10^{-2} \exp(-55\,000/RT) \text{ cm}^2\text{sec}^{-1}.$$

Die aus Umsetzungen in Pulversystemen bestimmte Diffusionskonstante bei 1300°C ist in annähernder Übereinstimmung mit diesen Messungen, was eine weitere Bekräftigung der Annahme darstellt, dass die Diffusion im Calciumorthosilikat in erster Linie geschwindigkeitsbestimmend ist für die Reaktion zwischen Calciumoxyd und Kieselsäure.

Die Ergebnisse der Selbstdiffusionsmessungen an den verschiedenen Calciumsilikaten sind schematisch in der Fig. 8 wiedergegeben. Wir sehen, dass in dem bei der Reaktion meistens untersuchten Temperaturintervall 1000° bis 1200°C die Selbstdiffusionskonstante von Calcium in Orthosilikat am höchsten, tiefer im $\text{Ca}_3\text{Si}_2\text{O}_7$ und im Metasilikat liegt. Nimmt man hierzu noch den Unterschied in der freien Bildungsenergie (39), die (bei 1140°K) für Calciumorthosilikat zu $28\,444 \text{ cal/Mol}$ und für Calciummetasilikat zu $20\,347 \text{ cal/Mol}$ angegeben wird, so ist die bevorzugte Bildung des Orthosilikates ausreichend erklärt (wenngleich auch noch andere Größen, wie Keimbildungsgeschwindigkeiten, eine Rolle spielen können).

Wie aus nachstehender kleiner Tabelle hervorgeht, steigt die Aktivierungsenergie für die Diffusion von Calcium mit zunehmendem Kieselsäuregehalt der Silikate, also zunehmender Verknüpfung der SiO_4 Tetraeder.

Die Selbstdiffusionskonstanten der Blei- und Calciumionen sind in verschiedenen Silikaten über grössere Temperaturbereiche gemessen und die Aktivierungsenergien ermittelt worden,

Tabelle 3. Aktivierungsenergien für die Selbstdiffusion von Calcium in verschiedenen Calciumsilikaten.

	α -Modifikation	β -(α')-Modifikation
Ca_2SiO_4	55	65
$\text{Ca}_3\text{Si}_2\text{O}_7$	(58)	73
CaSiO_3	112	(78)

wobei sich bei allen untersuchten Silikaten zeigte, dass bei zunehmender Verknüpfung der SiO_4 Tetraeder die zur (Ablösung und) Bewegung der Metallionen nötige Aktivierungsenergie ansteigt.

Die Beobachtung von JAGITSCH, dass der Wagnersche Reaktionsmechanismus bei der Bildung von Bleisilikaten nicht anwendbar ist, wurde qualitativ bestätigt; eine für die Gültigkeit des Wagnerschen Modells ausreichende Beweglichkeit von Siliciumionen ist in den bisherigen Versuchen nicht festgestellt worden. Im Fall der Calciumsilikate stimmen die Diffusionsmessungen gut mit dem Befund der bevorzugten Bildung von Orthosilikat bei der Reaktion zwischen Calciumoxyd und Kieselsäure überein; und die Diffusion von Calciumionen im Orthosilikat sollte hauptsächlich zeitbestimmend für die Bruttoreaktion sein.

Die Reaktionsformeln erfordern, falls Silicium nicht beweglich ist, auch einen Transport von Sauerstoff durch die Silikatschichten, eine Annahme, die bisher infolge der verhältnismässigen Grösse der Sauerstoffionen und der starken Si-O-Bindung unwahrscheinlich erschien.

Zur ergänzenden Untersuchung der Probleme erscheinen Diffusionsversuche mit dem langlebigen Si-32 angebracht, sowie solche zur Feststellung der Beweglichkeit von Sauerstoff mittels des Indikatorisotops O-18.“

Eine Zusammenstellung von Diffusionskoeffizienten in Pulvergemischen aus solchen Oxyden, die in der Glasindustrie angewendet werden, sind in zwei anderen Arbeiten von LINDNER (40) zu finden.

Im Vorhergehenden ist die grosse Bedeutung erwähnt von solchen Zuständen der festen Materie, wo neue Phasen entstehen und die Partikeln während einer Strukturänderung andere Beweglichkeit besitzen als nur Vibrationen oder ihre Transportrolle und Reaktionsfähigkeit wegen Strukturfehler erleichtert ist. Solche Zustände sind für kristallographische Umwandlungsprozesse, instabile Erbstrukturen, die z. B. bei thermischen Zerfallsprozessen auftreten, und in Festkörpern mit nicht gleichgewichtsmässig eingelagerten Gastpartikeln oder bei sonstigen Störungen charakteristisch. Im Vorhergehenden wurden Effekte dieser Art im Zusammenhang mit Umwandlungsvorgängen im SiO_2 und Ca-Silikaten genannt.

Solche Fälle wurden längst so vollständig studiert, dass es möglich war, die allgemeingültige Regel aufzustellen, dass *Feststoffe in Phasenübergangszuständen irgendwelcher Art eine erhöhte Reaktivität besitzen* (42).

Hier sollen nur folgende Beispiele zitiert werden, weil sie in unserem Zusammenhang von Interesse sind, und zwar nicht nur hinsichtlich Reaktionen zwischen Glaskomponenten sondern auch mit Rücksicht auf Korrosionsvorgänge zwischen Schmelze und Wannenmaterial. Untersuchungen, zum Teil mittels Emanations- und Radioisotop- und Röntgenmethoden, stellten fest, dass die Reaktionen zwischen CaO , MgCO_3 und CaCO_3 in Gemischen mit Kaolin, Feldspat, Glimmer, Sillimanit, Mullit, SiO_2 und anderen Oxyden bei Temperaturen anfangen oder erleichtert werden, wo zufolge Strukturumwandlungen oder thermischer Zerfallsprozesse neue Phasen ent-

stehen. In Anbetracht der Aktualität von TiO_2 -Zusätzen in modernen Glasprodukten soll auch auf das Ergebnis, dass die metastabile Anatasmodifikation und der unreine Rutil mit CaO leichter reagieren als die stabile, ganz reine Rutilform von TiO_2 (44).

Oben ist schon angedeutet, dass der Mechanismus von Reaktionen zwischen festen Phasen, und in vielen wichtigen Fällen auch in Systemen fest-flüssig oder fest-gasförmig, eine Reihe von immer noch ungelösten Problemen darstellt. Die ursprüngliche Vermutung von WAGNER, alle Umsetzungen auf Ionenwanderung zurückzuführen, ist wie erwähnt und auch von ihm anerkannt, nicht stichhaltig. Jede Adsorption oder Reaktion fängt natürlich an Oberflächen an, wo auch in Ionengittern VOLMER-DE BOERSche (45) molekülähnliche Gruppen von anderen Dipol- und Transportverhältnissen auftreten. Und unsere Kenntnisse von den grundsätzlich wichtigen Oberflächeneigenschaften sind in vielen Hinsichten sehr mangelhaft. Im Vorhergehenden wurde auch die ebenfalls sehr unvollständig untersuchten, bei steigenden Temperaturen zunehmenden Störungen durch Bildung von „Moleküloiden“ in thermisch dissoziierbaren Ionengittersubstanzen erwähnt. Auf ihre Rolle in reaktionseinwirkendem Sinne und die Fortpflanzung solcher Störungen vom Gitterinnern an die Oberfläche wurde vom Verfasser (46) und von RIEHL (47) aufmerksam gemacht.

JAGITSCH (48) hat im hiesigen Institut eine Reihe wichtiger Arbeiten über den Reaktionsmechanismus ausgeführt und mittels radio- und röntgenographischer samt Radioisotopmethoden in vielen Oxyd-Salz-Systemen nachgewiesen, dass jedenfalls an Phasengrenzen andere Partikelarten als Ionen den Umsetzungstransport besorgen. JAGITSCH hat dabei auch die Bedeutung der Korngrösse untersucht um das Verhältnis zwischen Phasengrenz- und innerem Diffusionstransport festzustellen (49). Reaktionskinetische Untersuchungen über die Rolle der Phasengrenzreaktionen, also die erste Stufe der Umsetzungen wurden auch von LINDNER mittels Radioisotopmethoden ausgeführt (50). In vielen Veröffentlichungen hat LINDNER und Mitarbeiter auch für oxydchemische Systeme wichtige Resultate mitgeteilt (51).

Zu dieser Problemgruppe gehört auch die äusserst komplizierte und unvollständig beantwortete Frage über den Mechanismus kristallographischer Umwandlungsvorgänge, deren Verlauf in den weitaus meisten unaufgeklärten Fällen mit Unterschieden zwischen den in Frage kommenden Strukturen, Fehlstrukturen und erbstrukturbeeinflussten Trägheitszuständen etc. zusammenhängt. Im Göteborger-Institut wurde auch dieses Problem aufgenommen, und für Silbersulfat, wo die Verhältnisse relativ leicht zu behandeln sind, hat JOHANSSON (52) seine Ergebnisse veröffentlicht.

Hiermit sehr nahe verwandt sind auch die Sintervorgänge. Ein grosses Experimentmaterial, dessen Ergebnisse zum Teil durch Versuche mit Glas erhalten wurden, liegt in verschiedenen Büchern und Zeitschriften vor, ohne dass es möglich wurde zu einer einheitlichen Erklärung oder allgemeingültige mathematische Formulierung der Kinetik zu gelangen. Zurückgreifend auf was oben über die komplizierten Vorgänge der Umsetzungsprozesse angeführt wurde, ist eine für alle Substanzen einheitliche Erklärung nicht zu erwarten (53).

Schliesslich soll in dieser Literaturübersicht die schon am Anfang aber auch im Folgenden dieser Arbeit beschriebene oft sehr beträchtliche Einwirkung von der umgebenden Atmosphäre auf Adsorptions- und Reaktionsvermögen, Sintern und Benetzbarkeit der Feststoffe genannt werden (54). Die oben beschriebenen Ergebnisse zeigen die grosse Rolle solcher Faktoren für die Herstellung und Behandlung — besonders beim Kühlprozess — des Glases. Im Folgenden ist gezeigt, dass auch die Reaktionsfähigkeit in Glaspulvergemischen davon abhängt.

Reaktionsversuche in Gemischen aus verschiedenen Glassorten und SrO, CaO und MgO

Angewandte Präparate

Kronglas

CaO = 12,0 %; MgO = 0,7 %; K₂O = 5,0 %; Na₂O = 9,5 %; SiO₂ = 71,6 %; Al₂O₃ = 0,7 %; Fe₂O₃ = Spuren. Glühverlust 0,2 %.

Daraus erhält man die „Seegerformel“:

0,493 CaO; 0,031 MgO; 0,122 K₂O; 0,354 Na₂O; 2,746 SiO₂; 0,015 Al₂O₃ und das „Molgewicht“ 228,8. Der „Transformationspunkt“ ca. 550°.

Jena Supremaxglas

BaO = 0,2 %; CaO = 5,1 %; MgO = 9,7 %; K₂O = 0,4 %; Na₂O = 1,1 %; SiO₂ = 58,9 %; TiO₂ = 0,1 %; Al₂O₃ = 23,5 %; Fe₂O₃ = 0,5 %; B₂O₃ = 0,6 %. Seegerformel: 0,004 BaO; 0,295 CaO; 0,629 MgO; 0,014 K₂O; 0,057 Na₂O; 3,183 SiO₂; 0,003 TiO₂; 0,747 Al₂O₃; 0,009 Fe₂O₃; 0,03 B₂O₃. „Molgewicht“ = 324,4 und „Transformationspunkt“ ca. 520°.

Ein Sr-Na-Glas eigener Herstellung

SrO = 11,3 %; Na₂O = 19,1 %; SiO₂ = 69,2 %; Al₂O₃ = 0,6 %; Seegerformel: 0,262 SrO; 0,738 Na₂O; 2,746 SiO₂; 0,015 Al₂O₃. „Molgewicht“ = 239,3. „Transformationspunkt“ ca. 480°.

Ein Pb-K-Glas eigener Herstellung

PbO = 32,7 %; K₂O = 13,8 %; SiO₂ = 53,5 %. Seegerformel: 0,500 PbO; 0,500 K₂O; 3,040 SiO₂. „Molgewicht“ = 341,1. „Transformationspunkt“ ca. 495°.

Ein Pb-Na-Glas eigener Herstellung

PbO = 37,4 %; Na₂O = 9,4 %; SiO₂ = 52,7 %; Al₂O₃ = 0,5 %. Seegerformel: 0,525 PbO; 0,476 Na₂O; 2,746 SiO₂; 0,015 Al₂O₃. „Molgewicht“ = 313. „Transformationspunkt“ ca. 500°.

Die Präparate der Zusatzoxyde (SrO, CaO und MgO) wurden in folgender Weise hergestellt:

SrO durch Erhitzung von SrCO₃ im H₂-Strom bei 1275°, wonach das gesinterte Produkt im Achatmörser gemahlen und wieder im H₂-Strom bei derselben Temperatur erhitzt wurde. — CaO durch Erhitzung von CaCO₃ im N₂-Strom bei 1000°. — Von MgO wurden durch Erhitzung des Hydroxyds oder Carbonats bei verschiedenen Temperaturen (ca. 400°, 6–700°, 1000°) verschiedene Präparate hergestellt. Sämtliche Ausgangs- und Endprodukte wurden auf Reinheit und erwünschte Zusammensetzung kontrolliert. Von den verschiedenen Gläsern wurden hinsichtlich ihrer Reaktionsfähigkeit mit den Zusatzoxyden drei Pulverpräparate (gesiebt durch ein Sieb mit 6400 Maschen) miteinander verglichen,

a) an der Luft im Trockenschrank 30 Min. bei 100° getrocknet (also unvollständig vom H₂O befreit);

b) vakuumbehandelt 3 Stdn bei ca. 550°, unter welchen Bedingungen das Glas nach SHERWOOD (8) vom aufgelösten H₂O befreit ist. Die Präparate wurden dann in einem Exsiccator einige Stunden intakt aufbewahrt;

c) im Autoklav 30 Min bei ca. 5 Atm. H₂O-Druck behandelt und vom Kondenswasser geschützt. Das Pulver war nach dieser Behandlung zu einem sehr harten Klumpf zusammengebacken und wurde daher im Achatmörser gemahlen, bei 40° 8 Stdn an der Luft „getrocknet“ und wie vorher gesiebt.

Moläquivalente (1:1) Mengen Glas + Zusatzoxyd wurden in Abwesenheit von CO₂ und H₂O in einem luftdicht geschlossenen Mischgefäß eingeführt und miteinander innig gemischt.

Unter denselben Vorsichtsmassregeln wurden dann (um Parallelwerte zu erhalten) zwei Pt-Schiffchen mit je 0,2 g Reaktionsgemisch in den zu der betreffenden Temperatur vorerhitzten Ofen nebeneinander eingeführt und 60 Min im trockenen CO₂-freien Luftstrom erhitzt. Danach wurden die reagierten Zusatzoxydquantitäten bestimmt.

Die Analysemethoden mussten zum Teil auxperimentiert werden, weil man genau darauf achtgeben muss, dass aus dem Glas nichts herausgelöst wird. Dies ist vor allem der Fall bei den MgO-Versuchen, weil MgO gegen Lösungsmittel sehr widerstandsfähig ist (in einem Fall, vgl. unten, musste auf angegriffenes Glas korrigiert werden).

Analytisches

Die unreaktierten SrO- und CaO-Mengen liessen sich auch einer etwas modifizierten Äthylenglykolatmethode (SCHLÄPFER-BUKOWSKI) bestimmen. Es wurde kontrolliert, einerseits dass man mit dem unreaktierten Gemisch 100 % freies Oxyd erhielt und andererseits, dass aus dem bei den verschiedenen Reaktionstemperaturen erhitzten Glas kein SrO oder CaO herausgelöst wurde. Etwa 0,1–0,2 g vom Reaktionsgemisch werden (zusammen mit einigen Quarzkörnern zum Zerreiben von Klümpchen) in einem Erlenmeyerkolben (300 cc) mit 40 cc absolut wasserfreiem und neutral reagierendem Äthylenglykol bei 65–70° $\frac{3}{4}$ Stdn geschüttelt. Danach wird durch ein Spezialnutschfilter filtriert, mit 50 cc wasserfreiem C₂H₅OH gewaschen und das Filtrat mit 0,1 N HCl und α -naftoltalein-fenoltalein (100 mg fenoltalein + 150 g α -naftoltalein + 100 mg abs. C₂H₅OH) als Indikator titriert.

Die Bestimmung des unreaktierten MgO ist etwas umständlicher. Nach vielen Versuchen erwies sich das Auslaugen des Reaktionsgemisches mit einer Lösung von Essigsäureanhydrid im abs. C₂H₅OH unter folgenden Bedingungen anwendbar. Es entsteht Magnesiumacetat nach: $\begin{smallmatrix} \text{CH}_3\text{CO} \\ \text{CH}_3\text{CO} \end{smallmatrix} > \text{O} + \text{MgO} = \text{Mg}(\text{OOCCH}_3)_2$. Weil ein Teil des Anhydrids unter Esterbildung mit dem Alkohol reagiert, ist ein genügender Anhydridüberschuss notwendig. Unter den in Frage kommenden Versuchsbedingungen zeigte es sich am besten eine Lösung anzuwenden, die nach vollständiger

Tabelle 4. Getrocknetes (Trockenschrank) Kronglas + MgO.

Reaktionstemp. °C	MgO reagiert in %	Mittelwert
400	– 0,6; 0,0	– 0,3
450	16,0; 13,1	14,5
500	16,6; 15,6; 15,0; 14,8	15,5
525	11,0; 12,4	11,7
550	11,2; 12,7	11,9
600	16,6; 15,3	16,0

Esterifizierung ca. 7.5 % freies Anhydrid enthielt. Durch Blindproben wurde festgestellt, dass dieses Lösungsmittel unter den im folgenden gegebenen Umständen erst nach etwa 2-stündigem Schütteln nennenswerte Alkalimengen aus dem Glas herauslöst. In den Versuchen mit dem bei 6–700° hergestellten MgO wurde während 60 Min und mit dem bei 1000° hergestellten Oxyd während 90 Min ausgelaugt.

Die Reaktionsprodukte wurden wie vorher in Erlenmeyerkolben mit dem Lösungsmittel in einem Thermostat bei 30° geschüttelt. Das ungelöste wurde in Goochtiegeln nach sorgfältigem Waschen mit abs. Alkohol vom Gelösten abgeschieden und gewogen. Die Gewichtsvermehrung des Tiegels bedeutet die unreaktierte MgO-Quantität.

Die Ergebnisse der Reaktionen mit den drei Oxyden (SrO, CaO, MgO) werden kurvenmässig gezeigt. Nur die Tabelle 4 über die Genauigkeit der MgO-Bestimmungen sei als Beispiel wiedergegeben. Die Unterschiede zwischen den Parallelversuchen sind, wie nach dem oben genannten, grösser als bei den SrO- und CaO-Versuchen, wo sie höchstens 0,5 % in der Regel nur einige 0,01 % betragen.

Reaktionsversuche mit SrO

(nach Expp. von G. LINDEMAN)

Die Versuche wurden mit Kronglas, Sr-Na-Glas und Pb-K-Glas ausgeführt. Wie aus den Figuren 9, 10 u. 11) ersichtlich, sind die umgesetzten SrO-Mengen mit jedem Glas sehr viel geringer wenn das Glas im Vakuum entwässert wurde. Aber auch diese

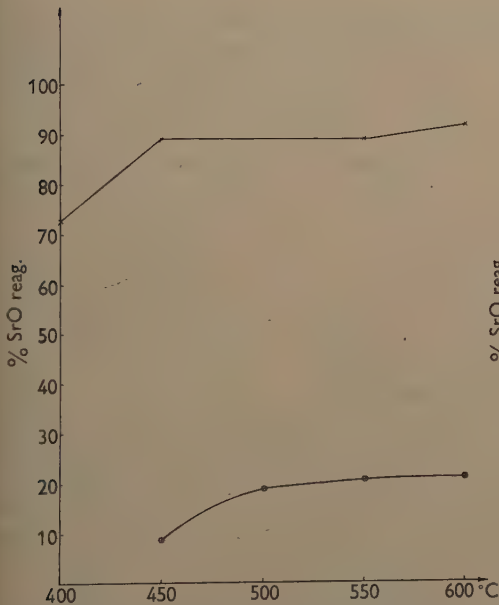


Fig. 9. Umsetzung zwischen SrO und Kronglas, entwässert im Vakuum 3 Stdn bei 550° (○); an der Luft aufbewahrt ohne Vorbehandlung und also wasserhaltig (x).

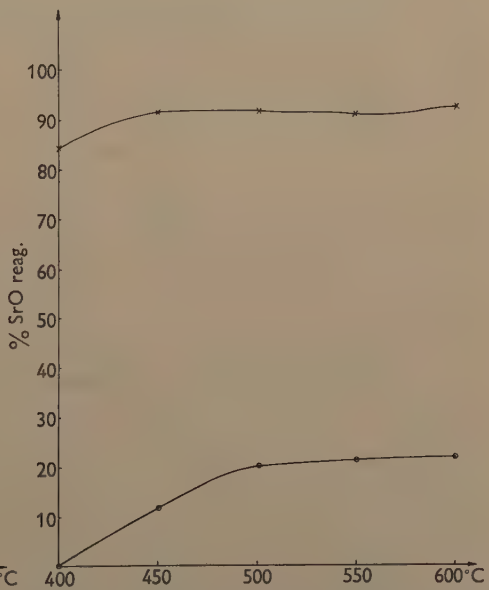


Fig. 10. Umsetzung zwischen SrO und Sr-Na-Glas, entwässert im Vakuum 3 Stdn bei 550° (○); „bewässert“ im Autoklav 2 Stdn (x).

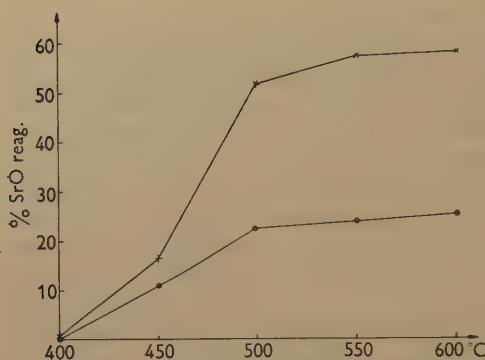


Fig. 11. Umsetzung zwischen SrO und Pb-K-Glas entwässert im Vakuum 3 Stdn bei 500° (O); „bewässert“ im Autoklav 2 Stdn (x).

Präparate geben verhältnismässig hohe Ausbeuten; in sämtlichen Fällen werden Höchstwerte von etwa 20 % (25 % für Pb-K-Glas) reagiertes SrO erreicht. Bei den Versuchen mit bewässerten Präparaten spielt bei den niedrigeren Temperaturen zweifelsohne die Bildung von $\text{Sr}(\text{OH})_2$ durch Reaktion zwischen SrO und das „Glaswasser“ und später die Zurückbildung von SrO eine Rolle (55).

Es hat ein besonderes Interesse, das SrO auch mit dem SrO-Na-Glas reagiert, was zweifelsohne mit dem hohen Alkaligehalt zusammenhängt (vgl. unten bei den CaO-Versuchen).

Der Einfluss eines Transformationsprozesses ist bei diesen Versuchen gering oder überhaupt diskutierbar (vgl. unten). Beim entwässerten Pb-K-Glas (Lindeman vgl. S. 333 unten a) tritt ein kleiner Puckel auf, und die Unterschiede zwischen den %-Zahlen bei den Parallelversuchen sind im Transformationsintervall ein wenig grösser als normal, ein Verhältnis, das bei allen strukturellen Umwandlungsvorgängen auftritt (56).

Wie erwähnt sind die reagierten Mengen wenigstens mit bewässerten Präparaten so hoch, dass Gläser mit so hohen %-Zahlen von SrO sicherlich nicht existieren. Wenn 90 % SrO mit dem ursprünglichen Sr-Na-Glas ($\text{SrO} = 11,3\%$) reagieren und das reagierte SrO im Glas als glasbildendes Oxyd verbleiben würde, hätte dieses Glas folgende Zusammensetzung: $\text{SrO} = 36,9\%$; $\text{Na}_2\text{O} = 14,1\%$; $\text{SiO}_2 = 49,0\%$. Ein solches Produkt ist als Glas nicht existenzfähig, sondern enthält ein Gemenge von auskristallisierten Verbindungen. Sogar unser Versuch, ein Glas mit ca. 20 % SrO herzustellen gelang nicht. Das Produkt war kristallisiert.

Bei den Experimenten mit entwässertem Glas hätten etwa 20 % SrO reagiert. Unter der Annahme dass diese 20 % SrO im Glas bleiben, würde man folgende Zusammensetzung bekommen: $\text{SrO} = 17,9\%$; $\text{Na}_2\text{O} = 18,1\%$; $\text{SiO}_2 = 64,0\%$. Die Segerformeln dieser beiden Gläser wären also: 0,612 SrO; 0,388 Na_2O ; 1,401 SiO_2 und 0,382 SrO; 0,618 Na_2O ; 2,355 SiO_2 bzw. Gläser mit so hohen Gehalt an Erdalkalioxyd wie letzteres und namentlich an SrO, sind uns nicht bekannt, erst recht nicht bei so einfach zusammengesetzten Gläsern wie die hier angewandten.

Wenn man nun weiter bedenkt, dass es bei den Reaktionen in erster Linie eine Frage von Umsetzungen in mehr oder weniger dicker Oberflächenschichten handelt, so erhellt, dass wir bei den hohen Umsetzungszahlen in diesem und anderen Mischungen nicht mit Reaktionen zwischen Zusatzoxyd und Glas zu tun haben sondern mit sogenannten Platzwechselaktionen zwischen dem Oxyd und kristallisierten Verbindungen. (Vgl. S. 327.)

Reaktionsversuche mit CaO

(nach Expp. von N. BRAUER)

Die Versuche wurden mit Kronglas, Supremaxglas und Pb-K-Glas ausgeführt.

Mit den entwässerten Kron- und Supremaxgläsern reagiert CaO nicht unter den angewandten Versuchsbedingungen. Dieser Umstand hängt wohl damit zusammen, dass das Kronglas schon recht viel CaO und das Supremaxglas ausserdem viel MgO enthält. Umsetzungen finden aber statt mit den alkalireichen Pb-Na- und Pb-K-Gläsern, wie aus den Figuren 12 u. 13 hervorgeht. In diesem Zusammenhang soll auch das Ergebnis (vgl. Reaktionsversuche mit SrO oben) erwähnt werden, dass SrO mit dem sehr alkalireichen Sr-Na-Glas reagiert (vgl. Fig. 12). Sämtliche diese Befunde scheinen im guten Einklang zu sein mit den Berechnungen von DIETZEL (57) über die Anziehungskräfte zwischen Kationen und dem Sauerstoffion im Glas.

Wie aus den Figuren 12 u. 13 ersichtlich reagieren die im Autoklav bewässerten Pb-Na- und Pb-K-Gläsern wie immer besser als die im Vakuum vom Wasser befreiten Präparate. Ferner steigen die reagierten CaO -Mengen mit längerer Autoklavbehandlung. Das Pb-Na-Glas enthielt nach 30 Min 3,7 % und nach 2-Stündiger Autoklavbehandlung 4,1 % H_2O . Die entsprechenden Zahlen für das Pb-K-Glas waren 4,9 und 9,2 %. Bei so grossen H_2O -Mengen, die wohl wenigstens zum Teil nicht chemisch gebunden sondern nur aufgelöst sind, ist anzunehmen, dass mit dem CaO zuerst Ca(OH)_2 gebildet wird. Bei steigender Temperatur wächst aber schnell der H_2O -Druck des Hydroxyds und erreicht bei etwa 550° den Atmosphärendruck (58). Es scheint allerdings nicht ausgeschlossen, dass ein Teil der grossen Reaktionsfähigkeit mit dem aus dem intermediär entstandenen Hydroxyd *in statu nascendi* gebildeten und fehlgebauten CaO zusammenhängt. Transformationsmaxima treten auf den Kurven nicht auf und sind nach S. 331 auch nicht notwendig zu erwarten, weil erstens die Spannungen der schnell gekühlten entwässerten Präparate unvollständig ausgeglichen sind und zweitens weil die komplizierten Verhältnisse durch Oberflächenänderung eine Rolle spielen.

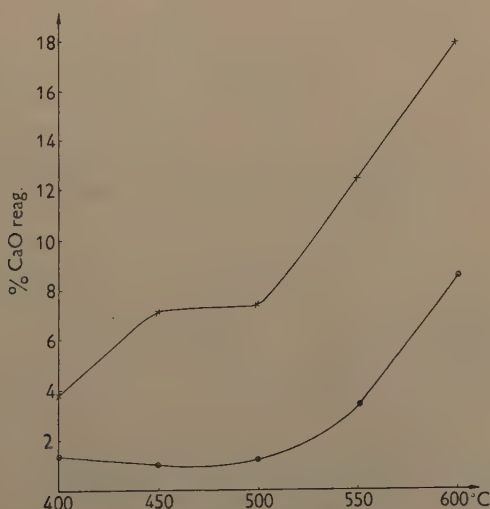


Fig. 12. Umsetzung zwischen CaO und Pb-Na-Glas, entwässert im Vakuum 2 Stdn bei 500° (○); „bewässert“ im Autoklav 5 Stdn (×).

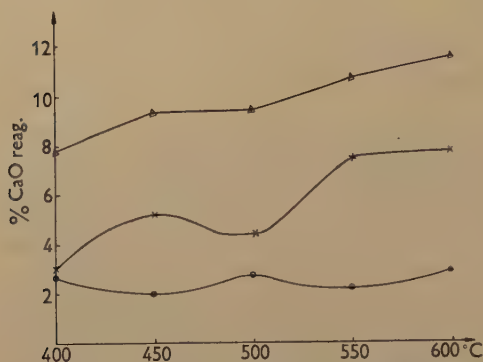


Fig. 13. Umsetzung zwischen CaO und Pb-K-Glas, entwässert im Vakuum 2 Stdn bei 500° (○); „bewässert“ im Autoklav $\frac{1}{2}$ Stde (×); 2 Stdn (Δ).

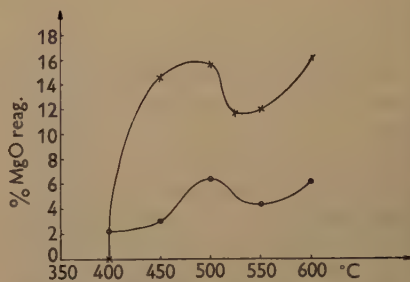


Fig. 14. Umsetzung zwischen MgO (400°) und Kronglas, entwässert im Vakuum 3 Stdn bei 600° (○); MgO (1000°) und Kronglas, entwässert im Vakuum 3 Stdn bei 600° (×).

Reaktionsversuche mit MgO

(nach Expp. v. P. BANE)

Die Versuche wurden mit Kronglas, Supremaxglas und Pb-K-Glas ausgeführt.

Auch in diesen Reaktionsgemischen sind die Umsetzungsbeträge mit wasserhaltigen Glaspräparaten sehr viel höher als mit den im Vakuum entwässerten. Es wurde in guter Übereinstimmung zwischen den Parallelversuchen der wasserhaltigen Präparate bis rund 50 % reagiertes MgO bei 600° gefunden. Dabei und auch bei viel niedrigeren %-Zahlen finden, wie oben bei den SrO-Experimenten erwähnt, Entglasung und sehr komplizierte Oberflächenreaktionen statt, und es hat natürlich keinen Zweck einen eindeutigen Einfluss vom Transformationsprozess zu erwarten.

Auffallend deutliche Umsetzungsmaxima treten aber auf, wie aus der Figur 14 ersichtlich, bei Erhitzungen von entwässerten Präparaten sowohl mit dem aus basischem Carbonat bei 1000° als auch mit dem aus Hydroxyd bei etwas über 400° hergestellten MgO (59). Es soll noch einmal unterstrichen werden, dass es, der Phasengrenzreaktionen und ev. Entglasungsvorgänge wegen, schwierig oder in vielen Fällen sogar nicht möglich ist, sichere Aussagen über die auf den Kurvenverlauf einwirkenden Faktoren zu machen. Wenn aber bei dem angewandten Kronglas die Zeit der Reaktionsversuche mit der Geschwindigkeit des Transformationsprozesses im Vorerweichungsgebiet etwas unter dem „Transformationspunkt“ harmonisiert, scheint es berechtigt von einem Zusammenhang zu sprechen. Es soll auch, wie schon mehrmals genannt, ausdrücklich hervorgehalten werden, dass Umwandlungsvorgänge an Oberflächen in der Regel bei niedrigeren Temperaturen verlaufen als in dem inneren Gittergefüge.

Beim ersten Blick auf die beiden Kurven (Fig. 14) sieht es aus als ob das bei viel höherer Temperatur hergestellte MgO besser reagiert als das aus dem Hydroxyd erzeugten. Dies hängt aber zweifellos damit zusammen dass letztere Werte zu niedrig sind, weil in diesem Falle die Behandlung mit der Essigsäureanhydridlösung so lange dauerte, dass das Glas selbst angegriffen wurde.

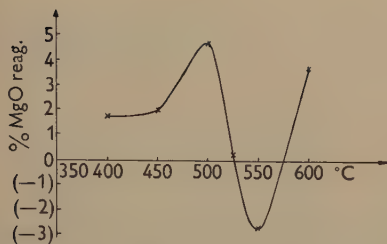


Fig. 15. Umsetzung zwischen MgO (1000°) und Supremaxglas, entwässert im Vakuum 3 Stdn bei 550° (×).

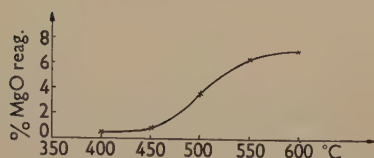


Fig. 16. Umsetzung zwischen MgO (1000°) und Pb-K-Glas, entwässert im Vakuum 2 Stdn bei 500° (×).

Ein solches Verhalten tritt besonders deutlich bei den Versuchen mit dem Supremaxglas hervor (Fig. 15). Das Maximum kurz unter dem „Transformationspunkt“ ist sehr deutlich, und hier darf man wohl einen direkten Einfluss von der Strukturänderung annehmen, weil die reagierten MgO-Mengen so klein sind, dass keine Entglasung stattfindet. Der Grund des negativen Umsetzungsbetrages wurde quantitativ bestimmt. Es zeigte sich nämlich, dass dieses entwässerte und schnell abgekühlte Supremaxglas bei der angewandten Bestimmungsmethode ein wenig angegriffen wurde (60). Bei sämtlichen %-Zahlen soll daher nach ausgeführten Kontrollversuchen eine Korrektur von ca. +3% angebracht werden.

Wie erwähnt wurden auch Experimente mit dem Pb-K-Glas ausgeführt. Dabei wurde, wie in allen Experimenten mit den Pb-Gläsern nicht nur dieselbe sehr grosse Erhöhung der Reaktivität im bewässerten Zustand sondern auch die ohne Maxima (Fig. 16) verlaufenden Umsatzkurven mit entwässerten Präparaten gefunden.

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Tryckt den 28 oktober 1958

On the mechanism of alkylation of β -keto esters

III. The degree of dissociation of some salts of β -hydroxycoumarilic ester in methanol

By INGEMAR FORSLAD

Brändström (1) has recently pointed out that on alkylation of the salts of β -keto esters both the ions and the ion-pairs can take part in the reaction.

Acree (2) and later Brändström (3) have shown that it is often possible to calculate the reactivity of the ions and the ion-pairs in a reaction if the degree of dissociation is known. Therefore we have measured this for the Li-, Na-, K- and bispiperidinium (BP)-salts of β -hydroxycoumarilic acid ethyl ester (HCE), which are intended to be used in a series of alkylation runs (4, 5). The salts have been chosen so that they cover a wide range of dissociation at suitable intervals. Quite identical conditions with those used in alkylation are of course impossible and the error arising thereby will be discussed later (5).

Measurements and calculations

The measurements were made in methanol at 50°C with a conductivity bridge. HCE was always used in 5 % excess (the same as in the alkylation runs). However, HCE does not perceptibly influence the measurements as its conductivity constitutes only 1 % of that of its Li-salt and was further depressed by common ions.

The degree of dissociation was calculated by the method of Marshall and Grunwald (6).

In this case the distance of the closest approach of free ions (9.22 Å) was bigger than the effective distance, $a = 1.67 - 3.13$ Å (Table 5), hence the formula

$$\frac{\Lambda}{\alpha} = \Lambda_0 - \frac{S_{\Lambda} \sqrt{\alpha c}}{1 + 2.303 S \sqrt{\alpha c}}$$

was used. S (the limiting slope of the Debye-Hückel equation) was calculated to be 2.1146 from the formula (7)

$$S = \frac{1.825 \times 10^6}{(DT)^{\frac{1}{2}}},$$

where the dielectric constant $D = 28.05$ (8). S_{Λ} (the limiting slope of Onsager's equation) was calculated from the formula (9)

$$S_{\Lambda} = \frac{8.20 \times 10^5}{(DT)^{\frac{1}{2}}} \times \Lambda_0 + \frac{82.4}{\eta (DT)^{\frac{1}{2}}}.$$

As the viscosity (η) of methanol at 50°C is equal to 3.95×10^{-3} poise (10)

$$S_{\Lambda} = 0.9501 \Lambda_0 + 219.10.$$

After simplifying, the following practical formula was used

$$\alpha = \frac{\Lambda}{\Lambda_0} \times \frac{1 + 4.870 \sqrt{\alpha c}}{1 + \Delta S \sqrt{\alpha c}},$$

where

$$\Delta S = 4.870 + \frac{0.9501 \Lambda_0 + 219.10}{\Lambda_0}.$$

When after successive approximations, a constant value of α was obtained, a better value of Λ_0 was calculated by a method of Brändström (3). The activity coefficient γ was obtained from the formula

$$-\log \gamma = \frac{S \sqrt{\alpha c}}{(1 + 2.303 S \sqrt{\alpha c})^{\frac{1}{2}}}.$$

The required values of $-\log \gamma$ were obtained by graphical interpolation from a $-\log \gamma$ vs. $\sqrt{\alpha c}$ diagram. The plot of $1/\alpha \Lambda_0$ against $c \alpha \gamma^2$ gives a straight line in the concentration region $(5-100) \times 10^{-4} N$, with the intercept equal to $1/\Lambda_0$. The whole procedure was repeated until the value of Λ_0 converges.

Results

The values obtained are given in Tables 1-4, where $1/\Lambda_0 = 1/\alpha \Lambda_0 - c \alpha \gamma^2 / K \Lambda_0$ are given in the third column. The value of c is given in mole/l with an accuracy better than 0.1 %. The accuracy of Λ is therefore restricted by the accuracy

Table 1. The degree of dissociation of the lithium salt.

$c \times 10^4$	Λ	$10^3/\Lambda_0$	$\alpha \times 10^2$
8.055	84.92	9.170	83.5
10.18	81.83	9.157	81.0
20.26	71.13	9.180	72.0
80.55	48.72	9.135	52.3
102.7	45.10	—	48.9
206.1	35.00	—	39.3
613.5	22.55	—	27.0
820.1	20.00	—	24.4
1024	18.03	—	22.2
1450	15.04	—	18.9
1793	13.31	—	16.9
2809	10.32	—	13.2

Table 2. The degree of dissociation of the sodium salt.

$c \times 10^4$	Λ	$10^3/\Lambda_0$	$\alpha \times 10^2$
1.856	117.5		
4.692	108.1	8.532	97.7
9.376	101.7	8.548	93.7
46.89	82.64	8.549	81.5
95.01	71.81	8.526	73.7
472.5	45.44	—	51.7
938.0	34.78	—	41.4

Table 3. The degree of dissociation of the potassium salt.

$c \times 10^4$	Λ	$10^3/\Lambda_0$	$\alpha \times 10^2$
9.964	109.0	8.182	96.2
22.39	102.5	8.156	93.7
45.56	93.94	8.197	88.6
91.42	84.36	8.192	82.9
112.6	81.44	8.165	81.1
229.1	70.76	8.113	73.9
904.2	46.86	—	53.5
1146	43.17	—	50.1

Table 4. The degree of dissociation of the bispiperidinium salt.

$c \times 10^4$	Λ	$10^3/\Lambda_0$	$\alpha \times 10^2$
2.060 ^a	114.8	8.314	98.7
2.599	114.4	8.295	98.7
5.771 ^a	115.2	8.287	97.7
6.795	110.5	8.261	97.6
7.307 ^a	110.1	8.270	97.5
9.257	108.3	8.285	96.7
11.72	106.4	8.307	95.7
14.49 ^a	105.4	8.269	95.6
22.67 ^a	101.2	8.295	93.5
22.88	100.9	8.296	93.3
47.31 ^a	94.79	—	91.0
51.34	93.86	—	90.5
92.41	87.38	—	87.5
92.79 ^a	87.28	—	87.4
114.8 ^a	84.54	—	85.9
126.6	83.60	—	85.5
236.1 ^a	75.27	—	80.7
240.8	74.95	—	80.5
924.9 ^a	57.97	—	70.0
987.6	55.96	—	67.8
1157	53.65	—	65.9

^a The first of two series.

Table 5. The equivalent conductance (Λ_0), the dissociation constant (K), the distance of the closest approach of ions in the ion-pair (a) and the radius of the cation (r).

Salt	Λ_0	$10^3 \times K$	a (Å)	r (Å)	$a - r$ (Å)
Li	109.2	2.704	1.67	0.68	1.0
Na	117.1	10.08	2.27	0.98	1.3
K	122.3	18.98	2.96	1.33	1.6
BP	120.7	21.24	3.13	$> 2^*$	~ 1

* The shortest radius of the non-spherical BP-ion, estimated from a molecular model.

of the conductivity measurements (0.2–0.3 %) which would be enough for the purpose intended.

The results are summarized in Table 5, where the radii of the cations are also compared with the parameter a (calculated from Bjerrum's table (11)) which might be interpreted as the distance of the closest approach of the ions in the ion-pair. Both a and r increase in the series $\text{Li} < \text{Na} < \text{K} < \text{BP}$. The equivalent conductances give the order for the mobility of the cations $\text{Li} < \text{Na} < \text{BP} < \text{K}$, indicating different solvation of the ions.

Even if the BP^+ -ion has difficulty in forming a chelate in the usual meaning with the β -keto ester, there seems to be a continuous increase in the degree of dissociation in the series, intimating the indistinct limit between chelate and ion-pair.

Experimental

Methanol was purified by redistilling absolute *p.a.* methanol from aluminium amalgam (12). The conductance κ varied between 4.1 and 7.3×10^{-7} at 50°C ; the maximum solvent correction tolerated was 2 %.

Ethanol was purified by the magnesium method (12).

β -Hydroxycoumarilic acid ethyl ester (HCE) was prepared according to (4).

Bispiperidinium bromide (BPBr) was prepared from pyridine and 1,5-dibromopentane (13). M.p. $328\text{--}329^\circ\text{C}$. Found (by Volhard titration) equ. wt. 233.4–234.9. Calc. 234.18. Solubility in 100 ml of methanol: 36 g at 20°C ; 110 g at 64°C ; of ethanol: 12 g at 20°C ; 40 g at 78°C .

Methanol solution of the bispiperidinium salt of β -hydroxycoumarilic ester (HCE). A concentrated ethanol solution of BPBr was added during vigorous stirring to an equivalent amount of 1 *N* ethanol solution of KOC_2H_5 . The ethanol was continuously distilled until BPOC_2H_5 began to precipitate. The cooled solution was then decanted through a tube fitted with a glass-wool filter and then analyzed for bromide volumetrically. If the bromide content was low, the solution was evaporated *in vacuo* to near dryness, diluted with methanol, and samples titrated. An equivalent amount (plus 5 % excess) of HCE solution was then added. If the solution was e.g. 0.2 *N* it contained 1–2 % ethanol. It was necessary to precipitate KBr from ethanol, however, as BPBr was the salt available and KBr was too soluble in methanol. By evaporating the ethanol solution so far

that BPOC_2H_5 coprecipitated the rest of KBr , it was possible to bring down the KBr content to $< 1\%$ (calculated on the BP-salt). This contamination of ethanol gives a somewhat incorrect value to the degree of dissociation of the most concentrated solutions, but does not influence the value of Λ_0 . Diluted solutions were prepared by not more than twice dilution for each solution. During preparation all solutions were protected by pre-purified N_2 and the concentration determined by weighing and calculated by taking the density of methanol at 50°C to 0.7650 (14).

Alkali salt solutions were prepared from their alkoxide solutions.

Conductivity measurements were made by bridge essentially similar to that described by Matell and Lindenfors (15). The ground-glass-stoppered conductivity cell (constant 0.2110) has greyed platinum electrodes and was immersed in a thermostat filled with paraffin oil with low viscosity and controlled at $50.00 \pm 0.01^\circ\text{C}$.

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On the mechanism of alkylation of β -keto esters

II. A method to determine the products formed by methylation of β -hydroxycoumarilic ester

By INGEMAR FORSBLAD

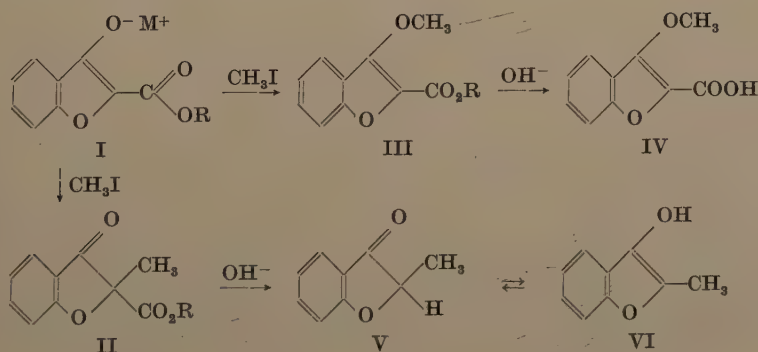
With 3 figures in the text

In an attempt to elucidate the mechanism of the alkylation of β -keto esters the methylation reaction of the β -hydroxycoumarilic acid ethyl ester (HCE) has been studied. HCE (I) is suited to the present purpose as it gives both C- and O-alkylation (II and III) and has earlier been the subject of a somewhat superficial investigation (1, 2). For kinetic purposes, however, we have to work out a suitable method to determine the velocity of the different reactions.

First HCE and its C- and O-methylated derivatives have to be prepared in pure form to be able to study their properties.

HCE has been prepared in pure enol-form by a modification of the method used by Friedländer (3) and Auwers (1), where factors such as high temperature and high polarity of the solvent, which promote the velocity of tautomerisation, were avoided (4).

Fig. 1 shows the IR-spectrum of the enol-form where the strong absorption at 5.98μ indicates a conjugated ester carbonyl which is strongly chelated to the enolic hydroxyl group. However, the substance also shows a very weak absorption band at 5.75μ indicating the presence of some percent non-chelating ester carbonyl. It is difficult to avoid tautomerisation during preparation of the sample as this reaction occurs rather rapidly at room temperature. After storing the substance a month at room temperature the band at 5.75μ grows to about the same intensity as the band at 5.98μ , Fig. 2, indicating that at equilibrium there are about equal quantities of both forms.



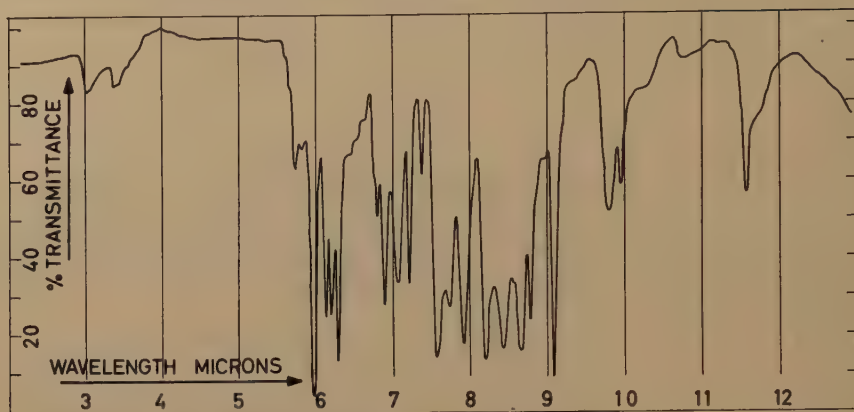


Fig. 1. IR-spectrum of β -hydroxycoumarilic acid ethyl ester in CCl_4 . (Perkin-Elmer 21 with NaCl prism.)

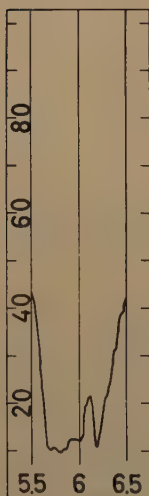


Fig. 2. IR-spectrum of ketonised β -hydroxycoumarilic acid ethyl ester in liquid phase.

Compared with cyclopentanone-2-carboxylic ester, which has its equilibrium strongly displaced in favour of the keto form (5), HCE has its enol-form more stabilized through the aromatic resonance energy in the furan ring. The same reason is also responsible for the still greater stability of the enol-forms of the S- and N-homologues, the 3-hydroxy-2-thionaphthen carboxylic ester and the indoxyl ester (2).

In this connection the surprising stability of HCE against alkaline hydrolysis can be mentioned, which was pointed out by Merriman (6) and Auwers (2). It can be boiled with alkali for two hours without any change, while its C- and O-alkylated derivatives and the acetoacetic ester are easily hydrolysed. In the anion of the compounds mentioned, the negative charge is distributed over the anion, reaching even the cationic centre of the carboxylic group. Therefore it is probable that only the undissociated molecule could be attacked by nucleophilic reagents.

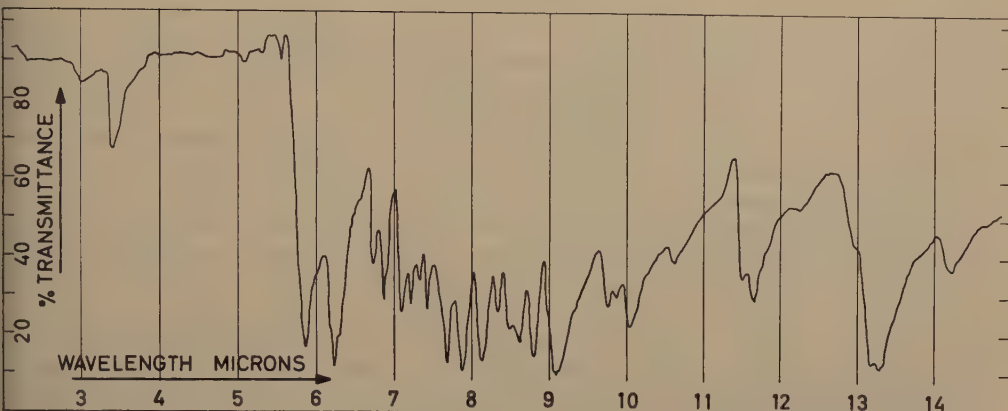


Fig. 3. IR-spectrum of β -methoxycoumarilic acid ethyl ester in pressed KBr.

As HCE is a stronger acid than the others the hydrolysis is rendered difficult as there are very few free ester molecules present in this case. The fact that acids easily hydrolyse all the esters mentioned supports this explanation.

The O-methyl derivative can easily be prepared through methylation by dimethyl sulphate (2) or better by diazomethane. The former agent probably gives some C-derivative. The elimination of the ability to chelate in the O-methyl derivative shifts the IR-absorption band of the ester carbonyl to 5.86μ (Fig. 3).

For synthesis of the C-methyl derivative there is no specific method and an attempt to separate it from the O-derivative by distillation (with a Todd's column (7) with 30–50 theoretical plates) failed. As the C-methyl derivative was only obtained as an oil, recrystallization was not an available method.

In order to follow the kinetic progress of the methylation reaction a spectrometric method would have been convenient but required both the methyl-derivatives in pure form. Therefore we were forced to use a chemical method, where we made use of the fact that the C- but not the O-derivative decarboxylates during saponification.

Now the method will be briefly described, then some of the details and the accuracy will be discussed.

The reaction velocity is measured at 50°C at a molarity of about 0.1 in alcohol solution with HCE and CH_3I in excess calculated on the alkali metal.

The methylation reaction is stopped by adding water and hydrochloric acid. The ester and its methylated products are extracted with CCl_4 . The residue is titrated to determine the velocity of the total reaction.

From the CCl_4 solution the unalkylated ester is extracted with KOH. The residue is saponified after evaporation and decarboxylated, then evaporated, acidified and the acid from the O-methyl product titrated. The difference between the rate of the total reaction and that of the O-alkylation is taken as the rate of the C-alkylation.

In spite of the much greater acidity of HCE compared with alcohol we use 5 % excess of the ester to depress the competing methylation of the alcoholate. However, to test if the decrease of the basicity during the reaction corresponds to the methylated ester formed, the titration method has been checked by

measuring HCE left behind by isolation, weighing and titration. Deviation was $<1.5\%$, the latter method giving some lower values. The evaporation of CH_3I during the run is shown to be very small, but to decrease the relative error caused by it CH_3I has been used in 100% excess.

To be sure that all HCE is present as enolic salt at the beginning of the reaction, HCE- and alkoxide-solution are first mixed and brought to constant temperature before adding the methyl iodide solution.

To prevent hydrolysis of the esters after the acid and the water has been added, the temperature is kept low and the extraction is made rapidly.

Among the extraction liquids heavier than water the esters are most soluble in CCl_4 .

The CCl_4 solution is rapidly extracted with KOH before any HCE has ketonised, as ketonization renders it difficult to remove all the unalkylated ester. Through the mild extraction procedure no O-methyl ester is hydrolysed.

During the following saponification, the O-product gives only β -methoxycoumarilic acid (IV) which does not decarboxylate below 100°C , while the C-product decarboxylates so easily that it is impossible to isolate.

There is, however, a possibility that the C-product could give O-(α -propionic acid)-salicylic acid by an acid hydrolysis. Auwers (1, 2) said it does not, but to test this the 2-methylcoumarone (V, VI) has been carefully removed from the saponification mixture by ether extraction and the acid was extracted with ether from the acidified residue. The β -methoxycoumarilic acid obtained after evaporation was not quite pure but was not contaminated with acidic substances. The values obtained by this control method agree within 5% with the usual method described above.

When Auwers studied the alkylation reaction he used water distillation to separate and determine the quantity of the products. However, we have found that it takes very long time to remove the 2-methylcoumarone from the strong alkaline mixture by ether extraction or water distillation as the enol-form of the ketone (VI) remains as salt. Attempts to regulate the pH by adding a buffer solution, so that the ketone but not the acid is removed proved, however, to be impracticable in the kinetic runs as the quantity and composition of the samples vary greatly.

Apparently it is therefore simpler to use a titrimetric method to distinguish the β -methoxycoumarilic acid from the 2-methylcoumarone. This is possible as the first acid is rather strong, pK_s determined to be 3.7, and the second is very weak. 2-Methylcoumarone is even a weaker acid than phenol and that probably depends on the greater stability of the exo- than the endo-double bond in five-membered rings (8, 9) which in this case compensates the loss of the aromatic energy. The pK_s of the ketone could not be determined as it is not soluble enough in water, but in alcohol solution at the concentration used in kinetic experiments it does not interfere with the titration of the β -methoxycoumarilic acid, which is completely neutralized at pH 6.5–7.0.

The method has been tested in several ways, including isolating the products formed after saponification.

As in methylation of HCE the C/O-alkylation ratio is about four and seems to be constant during the reaction, it is possible by several measurements during a reaction to get an accuracy better than $\pm 3\%$ for the rate of the C-alkylation and $\pm 5\%$ for the O-alkylation.

Experimental

β -Hydroxycoumarilic acid ethyl ester (HCE) was prepared by an improved method described by Brändström and Forsblad (4).

β -Methoxycoumarilic acid ethyl ester was prepared by methylation of HCE:

(1) According to Auwers (2) by dimethylsulphate. Two recrystallizations from light petrol gave in 31 % yield an ester with m.p. 57.0–58.5°C (Auwers found 59°C).

(2) By diazomethane. From 22 g of *p*-tolylsulphonyl methyl nitrosoamide an ether solution containing about 70 mmol of diazomethane was prepared according to de Boer and Backer (10). To that 10.3 g (50 mmol) of HCE was added and after standing at room temperature during one hour the ether was evaporated and the residue recrystallized once from light petrol. Yield 9.3 g (82 %), m.p. 64.5–66.0°C. Mixed with the product from method 1) gave m.p. 63.5–65.0°C and with HCE an oil.

Stability against saponification in heterogeneous systems:

0.5000 g (2.5 mmol) of *β -methoxycoumarilic acid ethyl ester* was dissolved in 100 ml of CCl_4 and stirred vigorously during three hours with 100 ml of 1 *N* KOH at 20°C. Afterwards the water-phase was acidified and continuously extracted with benzene overnight; the benzene solution evaporated and titrated. 0.85 % of the ester had been transformed into the acid and 99.3 % of the ester was recovered from the CCl_4 -phase.

The same experiment was repeated with ether instead of CCl_4 but treated only one hour. About 8 % of the ester was hydrolysed. The more rapid hydrolysis in the latter case probably depends on the mutual ether–water solubility.

β -Methoxycoumarilic acid was prepared by saponification of the ethyl ester according to Auwers (2). However, the same conditions were used as at analysing the kinetic runs. 1.100 g (5 mmol) of *β -methoxycoumarilic acid ethyl ester* was boiled with 0.95 g (15 mmol) of KOH dissolved in 15 ml of water–alcohol (1 : 5) and heated in the same way as in the analysis method described below. After boiling one hour about 70 % had been saponified but after 1½–2 hours 98–99 % of the acid could be recovered as shown by titration or by weighing. The acid was pale red-coloured and had a melting point not below 160°C. After recrystallization from ethanol m.p. 170–176°C (d) (Auwers found 166–170°C (d)).

Solubility and dissociation constant: Excess of the *β -methoxycoumarilic acid* was suspended in redistilled, boiled water in a stoppered bottle which was rotated in a thermostat at 20.0°C. Using a pipette with filtering device samples were withdrawn and titrated. When after seven days equilibrium was reached two 100 ml samples were titrated with 0.05000 *N* NaOH using a KPG-burette, holding 10 ml, and a pH-meter, Radiometer, type PHM 22a, with glass electrode. From the two titration curves the pK_s were determined to 3.65 and 3.74 respectively. The solubility was 25.0 mg/100 ml H_2O . The acid was very soluble in ether but very little in CCl_4 or CHCl_3 .

β -Methoxycoumarilic acid methyl ester. 1.00 g of *β -methoxycoumarilic acid* was added to a cold ether solution of diazomethane prepared (10) from 2.0 g of *p*-tolyl-

sulphonyl methyl nitrosoamide. After standing one hour the ether was evaporated and the ester recrystallized from light petrol forming colourless leaves, m.p. 82.0–83.0°C. Yield 0.81 g (75 %).

The analysis method

The description of the following run will serve as type for carrying out an analysis of the progress of the methylation:

About 50 mmol of alkali metal was weighed under dry light petrol and dissolved in 250 ml of methanol. Samples were titrated and calculated amount of HCE in 5 % excess was dissolved in 200 ml of methanol and added. The calculated amount of methyl iodide in 100 % excess was dissolved in about 200 ml of methanol. The amount of alcohol was taken so that the alkali concentration in the reaction mixture was 0.1 *N*. Before adding the methyl iodide solution both the solutions were brought to constant temperature $\frac{1}{2}$ hour at 50.0°C. All substances and solutions were weighed and the methanol was carefully purified (11). The reaction was carried out in a stoppered bottle.

Samples were withdrawn at intervals by a 50 ml pipette, previously warmed to 50°C and equipped with ground glass joints fitting the reaction bottle.

The sample was transferred to a $\frac{1}{2}$ l funnel which contained 200 ml of cold water, 5.00 ml of 1.200 *N* HCl and 50 ml of CCl₄ (purified by refluxing 2 hours with 5 % NaOH solution, then washed with water, dried and distilled (12)). The water-alcohol phase was further extracted twice with 25 ml of CCl₄ and then boiled for a few minutes, cooled and titrated with 0.2000 *N* NaOH until pH 5.3 (gray colour of bromcresolgreen + methylred).

The combined CCl₄ solutions were immediately extracted with 1 *N* KOH for 20 minutes, which was carried out in a tilted funnel equipped with an effective stirrer.

After standing 10 minutes the CCl₄-phase was separated and evaporated on a water bath through a 15 cm Vigreux column and refluxed 2 hours with 15 ml of 1 *N* KOH in water-alcohol (1:5) solution.

The alcohol was then evaporated and the residue cooled, acidified with 5 ml of diluted (1:1) H₂SO₄ (18 mmol) and extracted with 25 ml and then twice with 12 ml of ether. The ether extract was washed with $\frac{1}{2}$ ml of water and after complete separation the ether-phase was filtered through an ether-moistened paper and then evaporated, dried over NaOH in desiccator, then dissolved in 40 ml of alcohol and titrated with 0.2000 *N* NaOH from a 5 ml KPG-burette to green colour of bromthymolblue. The colour was compared with that of a K₂HPO₄–KH₂PO₄ solution with pH 6.8.

When other concentrations than 0.1 *N* were used in the reaction mixture the amount of the samples was regulated so that about 5 mmol were taken each time which was then diluted with four times more water than alcohol. For the rest the same conditions were used.

Testing of the method

Some of the most important experiments carried out to test the method are briefly described.

The rate of the total alkylation: A sample from a reaction mixture was treated

Table 1. Testing of the method for determination of the O-methylation.

Method	O-acid ^a calculated	O-acid ^a found	Per cent deviation
1 (3 samples)		1.614	± 1.5
2	2.084 ^b	2.184 ^b	+ 4.8
	2.064 ^b	2.092 ^b	+ 1.4
3 Weighing	1.614	1.664	+ 3.1
	1.614	1.689	+ 4.6
Titration	1.614	1.600	- 0.9
	1.614	1.624	+ 0.6
4	1.602	1.619	+ 1.1

^a O-acid = millimol. β -methoxycoumarilic acid.^b Based only on the β -methoxycoumarilic acid ethyl ester added.

in the usual way. However, after the extraction of the unalkylated ester with KOH solution, this solution was cooled and acidified to pH $\sim$ 2. The precipitated HCE was collected in a glass filter funnel and dried. The solution was extracted with ether. The extract was then dried and evaporated *in vacuo*. The combined HCE, which had the m.p. 61–66°C, was weighed and titrated. The value obtained was 0.93 % and 1.46 %, resp., lower than that obtained by the usual method.

The rate of the O-alkylation: From a reaction mixture the methyl iodide was removed by distillation and samples were analyzed in three ways:

(1) According to the usual method.

(2) According to the usual method but where a known amount of β -methoxycoumarilic acid ethyl ester had been added to the sample.

(3) By isolation of the products formed after decarboxylation. This was carried out in the following way: The saponification mixture was evaporated, neutralized with dilute H_2SO_4 and then buffered with a KHCO_3 – K_2CO_3 solution to pH 10.2. After three days of continuous extraction with ether all 2-methylcoumarone was removed and isolated from the dried ether solution and weighed.

The water solution was acidified, extracted continuously with ether for one hour. After the ether solution had been dried, it was evaporated and the crystallized β -methoxycoumarilic acid was weighed and then titrated to pH 8–10.

(4) In addition, an alcohol solution with a known amount of β -methoxycoumarilic acid was analysed in the usual way.

The results are collected in Table 1.

SUMMARY

A chemical method to determine the C- and O-alkyl products formed in methylation of β -hydroxycoumarilic acid ethyl ester has been worked out. Properties of some substances taking part have been analyzed and discussed.

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Studies on yeast invertase

VI. Inhibition by Ag^+ and the complexing of Ag^+ by yeast nucleic acid

By KARL MYRBÄCK and EBBA WILLSTAEDT

With 5 figures in the text

In a previous communication (1) it was shown that in crude invertase solutions, particularly autolysates of baker's yeast, impurities may be present which bind Ag^+ strongly and thereby protect the enzyme against the inhibiting action of the silver ions. Evidence was presented to show that this protecting action could be ascribed mainly to the presence of nucleic acids in the invertase solutions and that acid or alkaline hydrolysis of the nucleic acids practically abolished the protecting action, the degradation products of the nucleic acids having no or only a comparatively weak affinity for silver ions.

It could be shown that the protecting substances in crude invertase solutions are destroyed by papain. Since the papain preparation used was found to abolish also the protecting action of a yeast nucleic acid preparation, it could be concluded that the papain preparation contained traces of ribonuclease. To test this conclusion and to investigate the role of nucleic acids in the reaction of invertase preparations with Ag^+ , new experiments have been carried out, notably on the action of purified pancreatic ribonuclease on invertase preparations.

The *invertase* preparations used in these experiments have been described in an earlier publication (1). In the same paper are also described methods for measuring the *invertase activity* and for determination of the *protecting action* of impurities in the enzyme solutions or added substances.

Ribonuclease.—2 kg minced beef pancreas was mixed with 4 l 0.25 *N* sulphuric acid and left at $+2^\circ$ for 24 h with occasional stirring and then strained through cloth. The residue was mixed with 2 l 0.25 *N* sulphuric acid and treated in the same way. To the mixed extracts 430 g ammonium sulphate was added per liter; filtration at $+2^\circ$. 105 g ammonium sulphate was added per liter filtrate. After 45 h at $+2^\circ$ the precipitate was filtered off with suction. The filter cake (3.5 g) was dissolved in 17 ml water. 70 ml 25 % saturated ammonium sulphate solution, brought to pH 3 with sulphuric acid, was heated to boiling and the solution of ribonuclease was added. The mixture was kept at 97° for 5 min, cooled and filtered. The thoroughly dialyzed solution was called RNase I, dry weight 3.2 mg/ml.

RNase I, in amounts up to 3.2 mg, had no measurable protecting action on the Ag^+ inhibition of invertase (Table 1). This is in accord with the known fact, that pancreatic ribonuclease does not contain free HS-groups.

A number of experiments showed that treatment of invertase solutions of varying

Table 1. Protecting action on silver-inhibited invertase by yeast RNA, RNase I and RNA treated with ribonuclease.

[Ag ⁺]	Substance added	RA
—	—	1.00
—	1.05 mg RNA	1.00
5 × 10 ⁻⁶	—	0.06
5 × 10 ⁻⁶	1.05 mg RNA	0.72
5 × 10 ⁻⁶	1.05 mg RNA, treated with RNase I, 15 sec	0.11
5 × 10 ⁻⁶	1.05 mg RNA, treated with RNase I, 3 h	0.07
5 × 10 ⁻⁶	0.64 mg RNase I	0.06
5 × 10 ⁻⁶	3.20 mg RNase I	0.06

degree of purity with RNase at pH-values in the range pH 4–6 had no influence on the invertase activity.

RNase I had a very strong action on the protecting effect of yeast nucleic acid on silver-inhibited invertase: 10 ml solution of yeast nucleic acid (20 mg) was mixed with 2 ml RNase I and samples were taken at different times for the determination of the protecting action. Table 1 shows that the strong protecting action of the nucleic acid preparation was abolished in a few seconds.

Determination of protecting action

Action of RNase on invertase solutions

Experiments with Enzyme A 1

This enzyme solution (1) was prepared by ethanol precipitation of an autolysate of baker's yeast; activity 2.40/2 ml, dry weight 21.6 mg/2 ml, $If_{30} = 1.3$. Enzyme A 1 is rather insensitive to Ag⁺; the inhibition curve is shown in Fig. 1. 50 % inhibition is reached at $[Ag_{tot}] = 2.6 \times 10^{-5} N$, whereas purified invertase is 50 % inhibited at $[Ag_{tot}] \sim 10^{-6} N$.

210 ml Enzyme A 1 was treated with 1 ml RNase I at pH ~ 5 and 30°. After suitable times 2 ml samples were removed and the relative activity (RA) was determined at pH 5.3 in the presence of $1.5 \times 10^{-5} N$ Ag (Table 2). It appears that the sensitivity of the invertase solution to Ag⁺ increases strongly.

Table 2. Relative activity of Enzyme A 1, treated with RNase I.

pH = 5.3; $[Ag_{tot}] = 1.5 \times 10^{-5} N$.

Time of RNase treatment (days)	RA
0	1.00
3	0.45
6	0.22
9	0.12

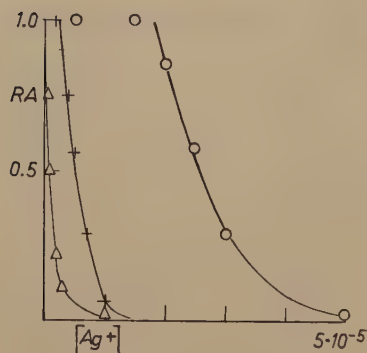


Fig. 1. Relative activity (RA) of invertase preparations at pH = 5.3 and various Ag⁺ concentrations: O, Enzyme A 1; +, Enzyme A 10; Δ, Enzyme B 200.

After 9 days the RNase-treated solution was dialyzed (*Enzyme A 10*, activity 1.60/2 ml, dry weight 13.8 mg/2 ml, If₃₀ = 1.4). The Ag-inhibition curve is shown in Fig. 1. For a comparison the inhibition curve of a highly purified yeast invertase solution (*Enzyme B 200*, If₁₈ = 200) is also shown in Fig. 1. It appears from the figure that the bulk of the protecting substances in *Enzyme A 1* have been destroyed by RNase.

Experiments with Enzyme A 4

The silver inhibition of this enzyme solution (activity 2.50/ml, dry weight 16.2 mg/ml, If₃₃ = 1.5) is shown in Table 3. 100 ml of the solution was treated with 1 ml RNase I at 30° and pH = 5. The Ag⁺ inhibition of 1 ml samples was determined (Table 3). For a comparison a 10 ml sample of *Enzyme A 4* was treated with papain at pH ~5 and 30°, and the silver inhibition of 1 ml samples was determined. Table 3 shows that RNase as well as papain destroy the protecting substances in *Enzyme A 4*. This is in accord with the assumption that the protecting substances in crude yeast invertase solutions are mainly ribonucleic acids and that degradation of these by

Table 3. Relative activity of *Enzyme A 4*, treated with RNase and papain, respectively.

pH = 5.3.

[Ag ⁺]	Treatment	RA
5 × 10 ⁻⁶	No treatment	1.00
1.2 × 10 ⁻⁵	No treatment	0.88
1.5 × 10 ⁻⁵	No treatment	0.59
1.7 × 10 ⁻⁵	No treatment	0.36
1.9 × 10 ⁻⁵	No treatment	0.21
2 × 10 ⁻⁵	No treatment	0.16
1.5 × 10 ⁻⁵	Treated with RNase, 16 h	0.05
5 × 10 ⁻⁶	Treated with RNase, 19 h	0.55
5 × 10 ⁻⁶	Treated with RNase, 70 h	0.45
5 × 10 ⁻⁶	Treated with RNase, 190 h	0.30
5 × 10 ⁻⁶	Treated with RNase, 360 h	0.25
5 × 10 ⁻⁶	Treated with papain, 50 h	0.30

Table 4. Relative activity of Enzyme A 4 treated with RNase at different pH values.

pH of assay mixture 5.3. $[Ag_{tot}] = 5 \times 10^{-6}$.

pH ...	3.97		4.91		5.95		6.62	
	a	b	a	b	a	b	a	b
Time of RNase treatment	Relative activity							
30 sec	1.00	—	1.00	—	1.00	1.00	1.00	0.94
1 h	—	—	0.76	1.00	—	—	0.71	—
3 h	0.88	1.00	0.47	—	0.36	1.00	0.36	0.94
6 h	0.88	—	—	—	—	—	—	—
24 h	0.68	1.00	0.35	1.00	—	—	0.20	—
48 h	0.60	1.00	—	—	0.22	1.00	—	0.89

ribonuclease practically abolishes the protecting ability, i.e. transforms RNA to products with a low silver-binding capacity.

The pH dependence of the RNase action on Enzyme A 4 was determined:

- (a) 7.5 ml Enzyme A 4 + 0.5 ml acetate buffer (N sodium acetate + acetic acid) + 1 ml RNase I, diluted 1:100 (32 μ g).
 (b) 7.5 ml Enzyme A 4 + 0.5 ml acetate buffer + 1 ml water.

The solutions *a* and *b* were kept at 20° under toluene. 1-ml samples were removed at certain time intervals and the relative activity was determined at pH = 5.3 in the presence of 5×10^{-6} N Ag^+ . Table 4 shows that the action of RNase on Enzyme A 4 is low at pH = 4, much higher at pH = 5 and still somewhat higher at pH 6–7. Experiments at pH values above 7 were not carried out since both invertase and ribonucleic acids are unstable in alkaline solutions.

Action of RNase I on yeast nucleic acid

A dialyzed solution of commercial yeast nucleic acid was used; it contained 1.10 mg/ml. For the determination of the protecting action on the Ag -inhibition of invertase experiments were carried out with Enzyme A 7 (activity 2.12/ml, dry weight 9.5 mg/ml, $If_{30} = 2.6$) at pH = 5.3 and $[Ag_{tot}] = 5 \times 10^{-6}$ N. 5 ml nucleic acid solution + 1 ml RNase solution, 30°. For the determination of the protecting action portions containing 0.92 mg nucleic acid were added in the inhibition experiments. Table 5 shows that already extremely small amounts of ribonuclease rapidly abolish the protecting action of RNA. Without RNase the nucleic acid solution is stable at pH = 4; at pH = 5.3 it seems to lose its protecting action slowly. However, the results were somewhat variable, and in most experiments no decrease in the protecting ability could be seen at pH = 5.3 without RNase. From Table 6 it appears that no such decrease could be observed even at pH = 5.95. This table illustrates the pH-dependence of the RNase action on yeast RNA:

- (a) 7.5 ml nucleic acid solution (0.95 mg/ml) + 0.5 ml acetate buffer + 1 ml diluted RNase I (1.3 μ g).
 (b) Same as (a), but water instead of RNase.

Portions corresponding to 0.93 mg RNA were added in the inhibition experiments. Table 6 shows that the action of RNase on the yeast nucleic acid used is strong at

Table 5. Decrease of the protecting action of yeast nucleic acid in the presence of RNase at 30°.

RA at pH = 5.3 and $[Ag_{tot}] = 5 \times 10^{-6} N$.

RNase ...	64 μg pH = 5.3	6.4 μg pH = 5.3	1.3 μg pH = 5.3	0 pH = 5.3	0 pH = 4.0
Time of RNase treatment	Relative activity				
15 sec	0.26	0.68	0.80	0.80	0.79
12 min	—	—	0.60; 0.63	—	—
1 h	—	0.26	—	0.74	—
2.5 h	—	—	0.24; 0.25	—	—
4 h	—	0.20	—	0.64	0.79
21 h	0.17	0.20	0.22	—	—
24 h	—	—	—	0.50	0.79

pH 5.3–6, somewhat less at pH = 5 and none at pH = 4. The pH-dependence of the enzyme action on yeast RNA thus is about the same as that of the action on the protecting substances in crude invertase solutions. The action on the latter seems to be somewhat slower than that on the preparation of yeast nucleic acid used in the experiments. Otherwise the experiments are quite in accord with the assumption that RNA is chiefly responsible for the protecting action of the impurities in the invertase solutions on the silver inhibition of the enzyme.

Table 6. Action of RNase at various pH-values.

The protecting action on Ag-inhibited invertase determined by measurement of RA at pH = 5.3 and $[Ag_{tot}] = 5 \times 10^{-6} N$.

pH ...	3.97		4.90		5.30		5.95	
	With RNase	Without RNase	With RNase	Without RNase	With RNase	Without RNase	With RNase	Without RNase
Time of RNase treatment	Relative activity							
15 sec	0.80	0.80	0.82	0.82	0.80	—	0.81	0.80
15 min	—	—	—	—	—	0.80	0.71	0.80
1 h	0.80	0.80	0.67	0.82	0.39	0.80	—	0.80
2 h	—	—	—	—	—	—	0.30	0.80
4 h	0.80	0.80	0.41	0.82	0.33	0.79	—	—
20 h	—	—	0.30	0.82	—	—	0.22	0.80
24 h	0.80	0.80	—	—	0.18	0.63	—	—

Spectrophotometric determinations

Action of RNase on yeast nucleic acid

The RNase action on yeast RNA was determined spectrophotometrically, using a Beckman spectrophotometer, model DU; light path 1 cm. All values are recalculated to a concentration of 0.05 mg RNA/ml or the corresponding concentration of degraded RNA.

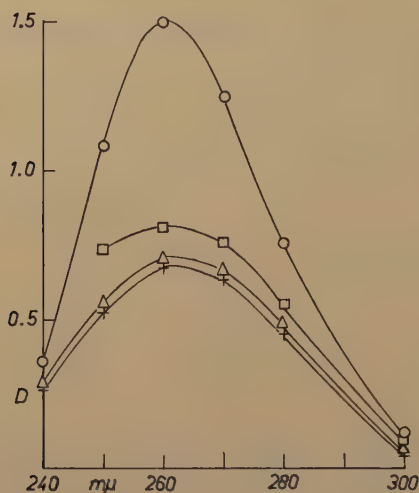


Fig. 2. UV absorption curves. Optical density (D) of (a) yeast ribonucleic acid, 0.05 mg/ml, $\circ$; (b) products soluble in MacFadyen's reagent after degradation of yeast nucleic acid by RNase: +, 15 sec.; Δ , 30 min; $\square$, 19 h.

The UV-absorption curve of the nucleic acid preparation used is shown in Fig. 2. The curve shows the typical maximum at about 260 $m\mu$.

To determine the maximal action of the RNase preparation 7.5 ml nucleic acid solution (0.95 mg/ml) was mixed with 0.5 ml acetate buffer, pH = 5.3, and 1 ml RNase I (3.2 mg) at 30°. 2 ml samples were pipetted into 2 ml MacFadyen's reagent (0.25 g uranylacetate and 2.5 g trichloroacetic acid in 100 ml); after 30 min the mixture was filtered and the filtrate was diluted to the desired concentration. A control in which the enzyme was added last to a mixture of RNA, buffer and reagent showed no absorption in the range 240–300 $m\mu$ when the values were corrected for the absorption of reagent and buffer alone. This correction has been applied in all determinations.

Fig. 2 shows that, at the very high enzyme concentration used, the reaction is practically complete in a few seconds. This is quite in accordance with the experiments on the action of a large amount of RNase on invertase solutions (Table 1). It is seen from Fig. 2 that even after prolonged action of the enzyme the UV-absorption is only about 50 % of that of RNA at the same concentration. This is also in accord with previous findings (2).

Since the products formed from ribonucleic acid by RNase have only a very weak protecting action against Ag-inhibition of invertase, it can be concluded that even

Table 7. Degradation of RNA at pH = 5.3 and 30°.

RNase	32 μ g	1.4 μ g	0
Time	Extinction at 260 $m\mu$		
15 sec	0.098	0.015	0.020
2 min	—	0.045	—
10 min	0.450	0.097	—
60 min	0.723	0.461	—
24 h	0.740	0.545	0.103

Table 8. Degradation of RNA at different pH values. UV-absorption of products soluble in MacFadyen's reagent.

pH ...	3.95	4.98	5.30	6.00
Time	Extinction at 260 m μ			
15 sec	0.067	0.061	—	—
10 min	0.083	—	0.097	0.128
30 min	—	0.135	—	0.246
60 min	0.129	—	0.461	—
20 h	0.121	—	—	—
24 h	—	0.396	0.545	0.445

comparatively high molecular (non-dialyzable) degradation products have a low Ag-binding capacity compared to that of ribonucleic acid.

Degradation experiments with smaller amounts of RNase were carried out at pH = 5.3 (Table 7). The increase of extinction at $\lambda = 260$ m μ was determined as above and recalculated to a RNA concentration of 0.05 mg/ml. The results are in good agreement with those obtained by determination of the protecting action on silver-inhibited invertase (Tables 4 and 5).

Some experiments were also carried out at different pH-values; method the same as above, 1.3 μ g RNase I, Table 8. These experiments are also in good agreement with those on the protecting action of RNA treated with RNase at different pH's. Table 8 shows a very slight action at pH = 4, which ceases rapidly, and a strong action in the pH range 5–6.

It was shown in a preceding paper (1) that treatment with papain strongly decreases the protecting action against silver inhibition of invertase by impurities in the crude enzyme solutions. It was also shown that papain destroys the protecting action of yeast RNA. The action of the same papain preparation on yeast RNA was also determined spectrophotometrically: 15 ml solution of yeast RNA + 1 ml acetate buffer, pH = 5.3, + 1 ml papain solution (2.3 mg), 30°. 2 ml samples + 2 ml MacFadyen's reagent. The filtrate was diluted to a concentration corresponding to 0.05 mg RNA/ml (Table 9) shows that yeast RNA is degraded by the papain preparation slowly but qualitatively in the same way as by pancreatic ribonuclease. Thus there is no doubt that the destruction of the protecting substances in the invertase solutions by papain is due to the presence of RNase in the papain preparation.

Table 9. Action of papain on RNA: UV-absorption of products soluble in MacFadyen's reagent.

Papain treatment ...	15 sec	24h	69 h	285 h
240 m μ	—	—	0.130	0.375
250 m μ	—	—	0.152	0.503
260 m μ	0.052	0.079	0.160	0.590
270 m μ	0.044	0.063	0.132	0.498
280 m μ	0.036	0.041	0.083	0.336
300 m μ	0.024	0.016	0.020	0.064

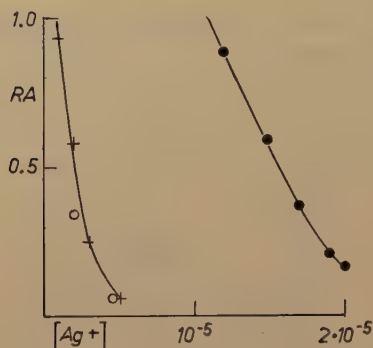


Fig. 3. Relative activity (RA) of invertase preparations at pH = 5.3 and various Ag^+ concentrations: ●, Enzyme A 4; +, Enzyme A 9; ○, Enzyme A 9 treated with RNase.

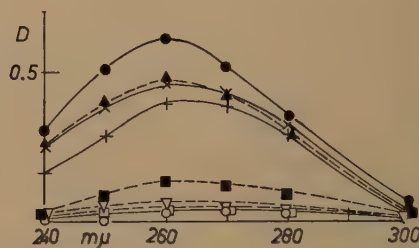


Fig. 4. UV absorption curves. Optical density (D) of (a) Enzyme A 4, 0.200 mg/ml, ●; (b) products soluble in MacFadyen's reagent after degradation by RNase: ○, 15 sec; +, 18 h; ×, 48 h; (c) products soluble in MacFadyen's reagent after degradation by papain: □—, 15 sec.; ▽—, 22 h; ■—, 68 h; ▲—, 285 h.

Spectrophotometry of invertase solutions

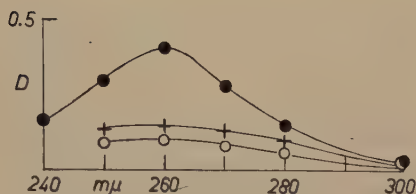
If nucleic acids are chiefly responsible for the protecting action of impurities in the crude invertase solutions, such solutions should be expected to exhibit the characteristic absorption about $260\text{ m}\mu$. Experiments were carried out with *Enzyme A 4*. The Ag-inhibition curve of this enzyme is shown in Fig. 3; it appears that the enzyme preparation contains large amounts of silver-binding impurities. The UV absorption in the range $240\text{--}300\text{ m}\mu$ of this solution (activity $2.50/\text{ml}$, dry weight 16.2 mg/ml , $\text{If}_{30} = 1.9$) was determined at a dilution of 0.200 mg/ml ; Fig. 4 shows the typical absorption curve of nucleic acid. A comparison with Fig. 2 allows the conclusion that the absorption of Enzyme A 4 at $260\text{ m}\mu$ corresponds to a content of about 0.019 mg nucleic acid/ml, i.e. about 10 % of the total dry weight.

The action of RNase I on Enzyme A 4 was determined spectrophotometrically: 7.5 ml Enzyme A 4 + 0.5 ml acetate buffer, pH = 5.3 + 1 ml RNase I, diluted 1:100, were kept at 30° . 2 ml samples were removed and mixed with 2 ml MacFadyen's reagent. The filtrates were diluted to a content of 0.200 mg Enzyme A 4/ml. The UV absorption values of table 10 and the absorption curves of Fig. 4 show that RNase

Table 10. Action of RNase I on Enzyme A 4.

Reaction time ...	15 sec	18 h	48 h
Density at			
$240\text{ m}\mu$	0	0.163	0.254
$250\text{ m}\mu$	0	0.288	0.380
$260\text{ m}\mu$	0.030	0.397	0.456
$270\text{ m}\mu$	0.033	0.385	0.430
$280\text{ m}\mu$	0.024	0.056	0.070

Fig. 5. UV absorption curves. Optical density (D) of (a) Enzyme A 9, 0.200 mg/ml, ●; (b) products soluble in MacFadyen's reagent, ○; (c) products soluble in MacFadyen's reagent after treatment with RNase for 48 h, +.



causes a considerable degradation of the nucleic acid to products, soluble in MacFadyen's reagent. This is quite in agreement with the observation that treatment of the enzyme solution with RNase abolishes the protecting action of the impurities on the Ag-inhibited enzyme.

Since the protecting substances in this and similar invertase solutions are destroyed by papain, the action of this enzyme was followed by determination of the UV absorption: 7.5 ml Enzyme A 4 + 0.5 ml acetate buffer, pH = 5.3 + 2.3 mg papain Merck was kept under toluene at 30°. 2 ml samples were precipitated with 2 ml MacFadyen's reagent, and the filtrates were diluted to a concentration corresponding to 0.200 mg invertase preparation per ml. The dashed curves of Fig. 4 demonstrate that the papain action on the invertase solution is slow but qualitatively the same as that of ribonuclease. This is also in accord with the results of the experiments on the abolition of the protecting action of impurities in the invertase solutions by papain action.

Spectrophotometrical determinations were also carried out on invertase solution A 9. This enzyme preparation (1) had the activity 0.84/ml, dry weight 2.32 mg/ml, $I_{f_{30}} = 4.3$. The Ag inhibition curve is shown in Fig. 3; it appears that, at least in comparison to Enzyme A 4, invertase solution A 9 contains only small amounts of protecting substances. The UV absorption of Enzyme A 9, diluted to a concentration of 0.200 mg/ml is shown in Fig. 5. A comparison with Fig. 2 permits the conclusion that the diluted solution of Enzyme A 9 contains about 0.014 mg/ml of substances having the same absorption curve in UV as yeast nucleic acid. This means that Enzyme A 9 contains about 7% "nucleic acid", and the question arises why this considerable amount apparently gives only a very weak protecting action against the silver inhibition of invertase (Fig. 3). The action of RNase on Enzyme A 9 was therefore examined.

15 ml A 9 + 1 ml acetate buffer, pH = 5.3 + 1 ml RNase solution I were kept at 30° for a time that should have been more than sufficient to bring any RNase action to completion. The Ag inhibition of the so treated solution was determined. Fig. 3 shows that the treatment with RNase has not brought about any considerable change of the sensitivity of the invertase preparation toward Ag^+ . This may be explained by one or both of the following assumptions: (a) Enzyme A 9 does not contain protecting substances in appreciable quantities, or (b) the substances of Enzyme A 9 showing UV absorption at 260 mμ are not broken down by RNase to any considerable extent.

The action of RNase on Enzyme A 9 was determined spectrophotometrically: (a) To a mixture of 15 ml Enzyme A 9, 1 ml acetate buffer of pH = 5.3 and 17 ml MacFadyen's reagent was added (last) 1 ml RNase I; (b) a mixture of 15 ml Enzyme A 9, 1 ml acetate buffer of pH = 5.3 and 1 ml RNase I was kept at 30° for 48 hours. Samples were mixed with an equal volume MacFadyen's reagent. The filtrates were diluted to a concentration corresponding to 0.200 mg invertase preparation. The results are shown in Fig. 5. It appears that part of the substances absorbing at 260 mμ

are not precipitated by MacFadyen's reagent and that the action of RNase increases this fraction only to a comparatively small extent.

As mentioned in this paper and earlier papers of this series, the action of RNase on yeast nucleic acid practically abolishes its protecting action on silver-inhibited invertase, i.e. its capacity of complexing silver ions in extremely diluted solutions. The experiments appear to indicate that the silver-binding capacity of yeast nucleic acid is decreased by RNase to a value, that may correspond to the complexing of Ag^+ by the mixture of mononucleotides that could be formed, theoretically, from the nucleic acid. However, it is well known that purified ribonuclease does not effect complete degradation of ribonucleic acid to mononucleotides, dialyzable oligonucleotides and non-dialyzable "limit polynucleotides" being formed in addition to pyrimidine mononucleotides. Our knowledge of the nature of the degradation products, other than the mononucleotides, is rather fragmentary and does not allow any conclusions concerning the complexing of Ag^+ by the various products. However, the experiments on the protecting action of the degradation products of yeast RNA on silver-inhibited invertase show that even the non-dialyzable products have a very low silver-binding capacity compared to that of yeast nucleic acid itself.

SUMMARY

The protecting action of impurities in crude yeast invertase solutions can be ascribed mainly to the presence of yeast nucleic acid. The ultraviolet absorption of such solutions in the range 240–300 $m\mu$ supports this conclusion. The action of purified ribonuclease on yeast nucleic acid and on the crude invertase solutions has been studied by measurement of the ultraviolet absorption of the degradation products soluble in MacFadyen's reagent. Degradation by ribonuclease practically abolishes the protecting action of yeast nucleic acid; the degradation products, dialyzable and non-dialyzable, have, compared to yeast nucleic acid, a very low silver-binding capacity.

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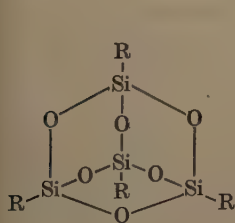
An improved method to prepare octa-(alkylsilsesquioxanes) (RSi)₈O₁₂

By KJELL OLSSON

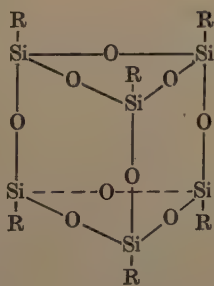
With 2 figures in the text

The products of the complete hydrolysis of alkyltrichlorosilanes may be formulated (RSiO_{1.5})_n and from an inorganic point of view regarded as oxides of alkylsilicon or as anhydrides of siliconic acids. They are usually described as amorphous non-volatile polymers in the literature. Recently, however, Wiberg and Simmler in a study of the hydrolysis of alkyltrichlorosilanes under special conditions (1) reported the preparation of compounds (RSiO_{1.5})₄ with the adamantane structure (I). The *tert*-butyl and *iso*-propyl compounds were obtained in good yields, but for R = ethyl, methyl or hydrogen (2) no low molecular products were isolated. Barry *et al.* prepared compounds (RSiO_{1.5})₈ (R = methyl, ethyl, *n*-propyl, *n*-butyl and cyclohexyl), for which they suggested the structure (III), by heating the hydrolysis products of the corresponding alkyltrichlorosilanes with alkali (3). One compound (RSiO_{1.5})₆ (R = phenyl) and one compound (RSiO_{1.5})₁₂ (R = methyl) were obtained in a similar way. A hexagonal prismatic structure was proposed for the latter compound. Sprung and Guenther in an extensive study of the partial hydrolysis of methyl- and ethyl-trialkoxysilanes (4, 5) obtained small amounts of the compounds (RSiO_{1.5})₆ and (RSiO_{1.5})₈ (R = methyl and ethyl), for which they suggested the structures (II) and (III) respectively. The compound (CH₃SiO_{1.5})₈ has probably been prepared before by Scott (6).

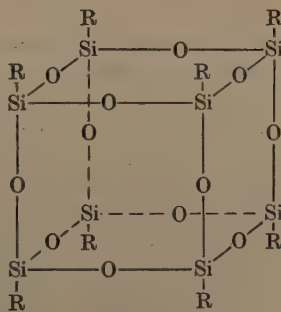
The purpose of the present paper is to report a simple and reliable method to prepare some of the compounds (RSiO_{1.5})₈ in relatively high yields. The yields of Barry *et al.* (3) are rather high, but their method is not very simple. Sprung and Guenther obtained the methyl compound in 10 % yield (5) but the ethyl compound in only 1.1 % yield (4).



I



II



III

My attention was originally drawn to these compounds by chance. From a "solution" of ethyltrichlorosilane in strong ethanolic hydrogen chloride, which was left at room temperature for about one month, a few large colourless crystals separated together with a heavy viscous oil. Analysis and molecular weight of the purified crystals agreed with the formula $(C_2H_5SiO_{1.5})_8$. When the experiment was repeated at reflux temperature, a yield of about 20 % was obtained, and the reaction time was shortened to a few days. On the basis of its melting point and other properties the compound was identified with that of Barry *et al.* (3) and with that of Sprung and Guenther (4) with the same empirical formula.

The reaction leading to the formation of the compound is probably complex, and a detailed interpretation has not been tried. Mechanisms which do not require the presence of water are conceivable. The initially formed ethyltriethoxysilane might e.g. react repeatedly according to the scheme



catalyzed by the strong acid present. Ethyltri-*n*-butoxysilane was therefore refluxed with several combinations of anhydrous solvents and acidic catalysts. Only very low yields of the desired product were obtained except for the solvents methanol and ethanol. This result suggests that water participates in the reaction, and that this water is gradually formed from reaction between alcohol and hydrogen chloride. The ethyltrialkoxysilane is then probably hydrolyzed by the water and the products of partial hydrolysis condensed as described by Sprung and Guenther (4). Since both the yield and the speed of reaction were greater in methanol than in ethanol, only methanol was used for further experiments. In these ethyltrichlorosilane was added directly to methanol without isolating the intermediate ethyltrimethoxysilane. High concentration of hydrogen chloride proved to be necessary for reasonably short reaction time.

That water is essential for the reaction was further stressed by the effect of adding small amounts of water to the reaction mixture from the start. The reaction was then greatly accelerated and the yield somewhat improved. Large amounts of water decreased the yield. The optimum yield was obtained with 1-6 times the theoretically required amount of water (1.5 moles per mole of ethyltrichlorosilane), but the yield was only slightly lower when 12 times this amount or no water was used. The optimum amount of water may depend on the proportion between ethyltrichlorosilane and methanol. As might be expected the yield was lowered in concentrated solutions owing to increased formation of polymers. The results thus gained in the preparation of the ethyl compound were directly applied to other alkyltrichlorosilanes and to phenyltrichlorosilane with only few additional experiments. The methyl compound was obtained in a higher yield when working at lower temperature and lower concentration of hydrogen chloride, but these findings were not applied to the less reactive higher alkyltrichlorosilanes owing to the strongly increased reaction time. The isolation of the compounds was simplified by their very slight solubility in methanol. The yields obtained and the melting points of the products are collected in Table 1.

The speed of the reaction decreases rapidly when R passes along the series methyl > ethyl > *iso*-propyl > *tert*-butyl. The same is to a smaller extent true about the series ethyl > *n*-propyl > *n*-butyl. Phenyltrichlorosilane reacts a little faster than ethyl-

Table 1. Yields and melting points of $(\text{RSi})_8\text{O}_{12}$.

R	Yield in %	M.p. (corr.)
Methyl	37	—
Ethyl	37–39	282–285°
<i>n</i> -Propyl	44	216–218°
<i>n</i> -Butyl	38–39	73–76°
<i>iso</i> -Propyl	17	295–300°
Phenyl	9	—

trichlorosilane. From *tert*-butyltrichlorosilane no product was obtained even after refluxing for 5 days. The relatively low yield of the *iso*-propyl compound was probably in part due to incomplete reaction in spite of refluxing for 8 days. *n*-Amyl- and *n*-hexyl trichlorosilane yielded only oils.

The identity of the products mentioned in Table 1 was secured by analyses and determinations of the molecular weights. The latter could not be determined by conventional methods for the methyl and phenyl compounds owing to their small solubilities. However, Mr. K. Larsson at the Inorganic Department of this Institute is carrying out an X-ray study of these compounds. He will present his results in detail in a separate publication. With his permission the following data are given here.

The methyl, ethyl and phenyl compounds all form rhombohedral crystals. The cell dimensions, a and α , and densities, d , determined by the flotation method, are collected in Table 2, which also contains the numbers, n , of formula units $\text{RSiO}_{1.5}$ in the cell, calculated from the cell dimensions and densities.

The obtained n values allow only two alternatives. Either the cell contains one single molecule $(\text{RSiO}_{1.5})_8$ or two molecules $(\text{RSiO}_{1.5})_4$. (The possibility of four molecules $(\text{RSiO}_{1.5})_2$ can, of course, be excluded without discussion.) Apart from other existing arguments against the adamantane structure $(\text{RSiO}_{1.5})_4$ (I) this could certainly not account for the identity in crystal form with the higher alkyl compounds, for which the formula $(\text{RSiO}_{1.5})_8$ has been established by current methods. The cell dimensions of the ethyl compound, which agree with those reported by Barry *et al.* (3), are included in Table 2 for comparison. Hence the formula $(\text{RSiO}_{1.5})_8$ is definitely established also for the methyl and phenyl compounds.

The infra-red spectra of all the compounds have been recorded in the region 2–25 μ . The absence of hydroxyl groups has been demonstrated in every case. From the spectra the presence of methoxyl groups cannot be excluded, however, since their absorption may be masked by the very strong Si–O absorption band at 9.0 μ (1110 cm^{-1}). The spectra of the methyl and phenyl compounds (in pressed KBr) are shown

Table 2. Cell dimensions, densities and cell contents of some compounds $(\text{RSi})_8\text{O}_{12}$.

R	a in Å	α	d in g/cm^3	n
Methyl	8.43 ± 0.01	$96^\circ 20' \pm 50'$	1.49 ± 0.01	7.9 ± 0.1
Ethyl	9.45 ± 0.01	$95^\circ 40' \pm 50'$	—	—
Phenyl	10.95 ± 0.02	$96^\circ 50' \pm 50'$	1.34 ± 0.01	8.0 ± 0.1

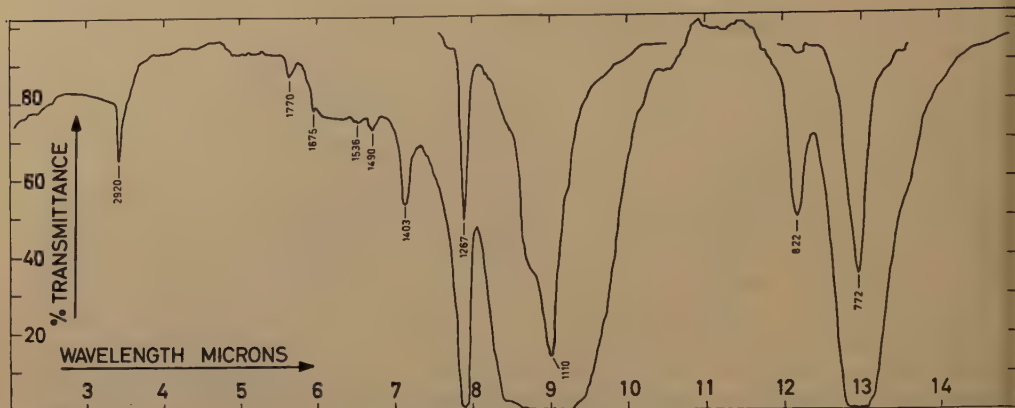


Fig. 1a. IR-spectrum of octa-(methylsilsesquioxane) (in pressed KBr) in the region 2–15 μ . The wavenumbers corresponding to the absorption peaks are given.

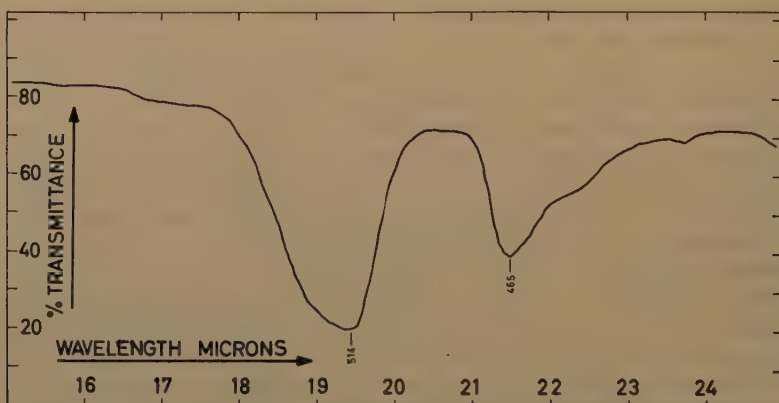


Fig. 1b. IR-spectrum of octa-(methylsilsesquioxane) (in pressed KBr) in the region 15–25 μ . The wavenumbers corresponding to the absorption peaks are given.

in Fig. 1 and 2 respectively. Owing to the tremendous intensity of the absorption bands involving silicon, and also since the vibrations of C–H linkages adjacent to silicon are weak (cf. e.g. Bellamy (7)), curves have been recorded for different concentrations.

In addition to the CH₃ vibrations at 3.42 and 7.13 μ (2920 and 1403 cm⁻¹) the following assignments for the methyl compound seem sure (7): 7.90 μ (1267 cm⁻¹) Si–CH₃ rocking, 9.01 μ (1110 cm⁻¹) Si–O stretching and 12.95 μ (772 cm⁻¹) Si–CH₃ stretching vibration. In the phenyl compound the peaks at 3.35, 6.25, 6.36, 6.71 and 14.37 μ (2990, 1600, 1572, 1491 and 696 cm⁻¹), the weak peaks in the region 5–6 μ (2000–1660 cm⁻¹) and the peak at 13.38 μ (747 cm⁻¹) with the shoulder at 13.51 μ (740 cm⁻¹) (which appears as a separate peak in Nujol) correspond to the usual vibrations of the phenyl group. The peaks at 6.97, 9.70 and 10.01 μ (1434, 1031 and 999 cm⁻¹) are characteristic of the Si–C₆H₅ group (7). The same is probably true about the peak at

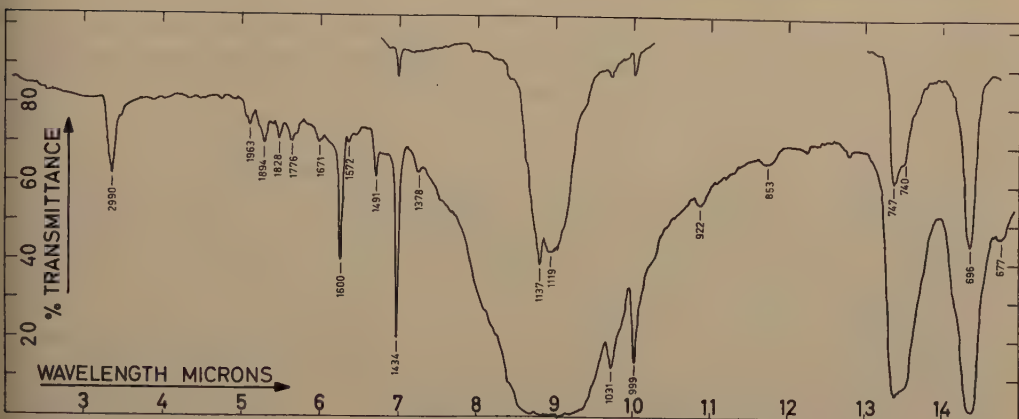


Fig. 2a. IR-spectrum of octa-(phenylsilsesquioxane) (in pressed KBr) in the region 2–15 μ . The wavenumbers corresponding to the absorption peaks are given.

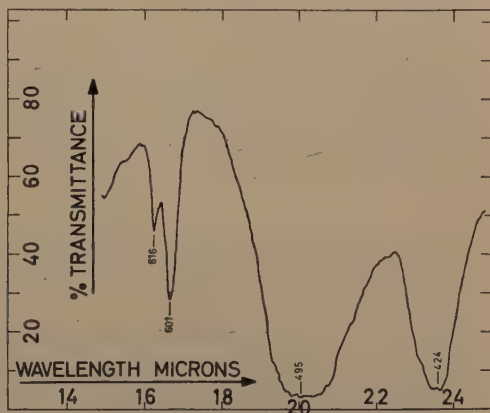


Fig. 2b. IR-spectrum of octa-(phenylsilsesquioxane) (in pressed KBr) in the region 15–25 μ . The wavenumbers corresponding to the absorption peaks are given.

8.80 μ (1137 cm^{-1}), which is almost overlapped by the very strong absorption band caused by the Si–O stretching vibration and with maximum at 8.94 μ (1119 cm^{-1}).

The relatively simple spectrum of the methyl compound is consistent with the high symmetry of the molecule. The spectra of the higher alkyl compounds are somewhat more complicated. The intensity and position of the Si–O band at about 9.0 μ (1110 cm^{-1}) are not changed, however. For the aliphatic compounds the maximum is on the average situated at 8.95 μ (1117 cm^{-1}) in chloroform solution and at 9.04 μ (1106 cm^{-1}) in pressed potassium bromide.

The properties of the methyl and ethyl compounds agree completely with those reported by Barry *et al.* (3) and by Sprung and Guenther (4, 5). The methyl compound already slowly decomposes at 270° . When gradually heated to 540° in a sealed tube it suffers no visible change, but when kept in this way at 350° for 5 minutes, only about half of the substance can be sublimed in vacuo afterwards. This decomposition may, however, be too slow to affect the vapour density determinations of Sprung and Guenther at 415° (5). The ethyl compound also decomposes

slowly at its melting point, whereas the *iso*-propyl compound is almost stable. Barry *et al.* found that the *n*-propyl compound decomposes very slowly even at 150° (3). The difficulty of obtaining quite sharp melting points is probably related to this slow decomposition. At least for the *n*- and *iso*-propyl compounds this is, however, mainly due to polymorphism.

The *n*- and *iso*-propyl compounds are very similar to the ethyl compound in every respect. As may be expected from the melting points, the *iso*-propyl compound is slightly less and the *n*-propyl compound slightly more soluble than the ethyl compound. The melting point of the *n*-propyl compound agrees with the value 219–220° reported by Barry *et al.* (3).

On the other hand the phenyl compound resembles the methyl compound. Thus it is very sparingly soluble in most solvents and decomposes on heating without melting. In contrast to the alkyl compounds it is not noticeably volatile.

The *n*-butyl compound is still more soluble than the *n*-propyl compound. The melting point is much lower than the value 190–195° reported by Barry *et al.* (3), and seems unexpected considering the melting points of the ethyl and *n*-propyl compounds. Since polymorphism had been revealed in some of the homologues, the *n*-butyl compound was kept for hours above its melting point in order to induce the crystallization of an eventually existing higher melting modification but with no success. The shape of the crystals is very similar to or identical with that of the other compounds. The possibility of an incompletely cyclized intermediate still containing a few methoxyl groups is hardly consistent with the analysis, which agreed perfectly with the formula $(C_4H_9Si)_8O_{12}$, as did also the molecular weight. As mentioned before, the infra-red spectrum excludes the presence of silanol groups.

Experimental

All temperatures in this paper concerning melting points are corrected, but boiling points are not.

Materials

Ordinary commercial methanol of “purum” grade was used. The term “methanolic hydrogen chloride” used below refers to methanol saturated at 0° with dry hydrogen chloride, kept in the refrigerator and used within two weeks.

Methyltrichlorosilane was purchased from Hopkin and Williams Ltd (“purum”) and distilled, b.p. 66–67°. Phenyltrichlorosilane was purchased from Fluka Ltd (“technical”) and used without purification. Attempts to prepare *tert*-butyltrichlorosilane according to Tyler, Sommer and Whitmore (8) met with no success, since *tert*-butylchloride failed to react with lithium in pentane. *tert*-Butyllithium could easily be prepared in ether solution at low temperature according to Bartlett and Lefferts (9), but in this solvent it yielded mainly high-boiling products with silicon tetrachloride; either this was added to the *tert*-butyllithium or vice versa. In this way only a few grams of impure *tert*-butyltrichlorosilane, b.p. 130–140°, were obtained, which was used directly after cooling to room temperature and decanting a few drops of liquid. The remaining alkyltrichlorosilanes were prepared according to the Grignard method. The following fractions were used:

ethyltrichlorosilane	b.p. 96–102° (mainly 98–100°),
<i>n</i> -propyltrichlorosilane	b.p. 122–124°,
<i>n</i> -butyltrichlorosilane	b.p. 146–149°,
<i>iso</i> -propyltrichlorosilane	b.p. 118–121°.

Ethyltri-*n*-butoxysilane was prepared by adding 1 mole of ethyltrichlorosilane to 4 moles of *n*-butanol with stirring and cooling in ice-water and distillation in vacuo, b.p. 123–126°/11 mm (mainly 124–125°).

Sublimation apparatus

The sublimation apparatus mentioned below was a Pyrex tube of 2½ cm inner diameter sealed in one end. The other end was narrowed in order to fit the rubber tube from the water pump. The apparatus was divided into a container and a receiver by a ground glass joint situated in the middle of the Pyrex tube. This fitted into an electrically heated furnace, so that the ground glass joint was barely inside the furnace. This was slightly inclined to prevent liquid in the container from flowing into the receiver. This simple apparatus proved to be very convenient for amounts of 0.2–20 g. The sublimation of smaller amounts was carried out in a test tube placed inside the apparatus with the open end 7–8 cm outside the furnace.

Preliminary experiments

4.3 g (5.0 ml) of ethyltri-*n*-butoxysilane was refluxed for 24 hours with 45 ml of solvent and usually 5–10 g of catalyst. Among solvents used were *n*-butyl ether, glacial acetic acid, absolute formic acid, acetic anhydride, xylene, absolute ethanol, methanol and dioxane. Among catalysts used were HCl, ZnCl₂, AlCl₃ and HClO₄. When the solvent was neither methanol nor ethanol, little or no sublimable product was obtained.

Octa-(ethylsilsesquioxane), (C₂H₅Si)₈O₁₂

To 110 ml of methanol in a 250 ml flask are added, while swirling by hand, first dropwise 6.2 g (5.0 ml) of ethyltrichlorosilane, then rapidly 70 ml of methanolic hydrogen chloride and finally rapidly 5.0 ml of conc. (aqueous) hydrochloric acid. The solution is refluxed for at least 12 hours and then left in the refrigerator for 24 hours. The supernatant liquid is carefully decanted and discarded. (If the hot solution is decanted immediately, the yield will be only slightly lowered.) The crude product is washed once with methanol and dissolved in a small amount of ether. The solution is transferred to the container of the sublimation apparatus, and the ether carefully removed on the water bath. The residue is gradually heated to 225° at 10 mm Hg and kept at this temperature for 30 minutes. About 1.8 g of crystals sublimes into the receiver. The contents of the container solidify on cooling to a transparent resin of polysiloxanes. In order to remove lower volatile siloxanes the sublimate is recrystallized from 85–90 ml of acetone. Yield 1.15–1.20 g (37–39%). For analysis the product was recrystallized once more from acetone and sublimed in vacuo.

C₁₆H₄₀Si₈O₁₂ (649.2) calc. C 29.60, H 6.21;
found C 29.65, 29.74, H 6.24, 6.15.

The molecular weight was determined ebullioscopically in benzene to 580, in chloroform to 590 and in ethyl acetate to 660. The camphor method of Rast yielded 710. The calculated value is 649.

In a series of experiments run as above but with varying amounts of (aqueous) hydrochloric acid the yields shown in Table 3 were obtained. In the second column

Table 3. Relation between the yield of $(C_2H_5Si)_8O_{12}$ and the amount of initially added water.

Conc. HCl in ml	Water (see text)	Yield in %
0.0	0.0	31
1.4	1.0	36
4.2	3.0	39
6.5	4.6	38
8.4	6.0	38
16.8	12	33
33.6	24	26

the water of the hydrochloric acid is expressed using the theoretically required amount as unity. The refluxing was continued for 45 hours in order to assure complete reaction.

In addition to the characterization already given by Barry *et al.* (3) and by Sprung and Guenther (4) some details will be pointed out. The ethyl compound forms well-defined rhombic prisms. By evaporation of an ethereal solution cm-long crystals are easily obtained. When placed in a sealed tube in a melting point apparatus preheated to 280° and adjusted to a rate of heating of 1° per minute the compound melts at 282–285°. If first kept for 1½ hours at 285° it melts very unsharply, and a clear melt is already formed at 267° due to partial decomposition. Obviously another modification melting at about 260° exists, for when a sample recrystallized from acetone is heated slowly, it melts almost completely at this temperature, then solidifies at about 275° and finally melts at 281–284°. A sublimed sample does not behave in this way, probably because it contains crystals of the higher melting modification, which induce a direct transition between the solid phases.

The compound suffers no change when refluxed for 1 hour with fuming nitric acid or aqua regia, when treated with hot perchloric acid or when treated with bromine in carbon tetrachloride solution. It is attacked by conc. sulphuric acid only at high temperature. Heating with phosphorus pentachloride seems to have no effect. It is not altered when refluxed for 1 hour with 60 % aqueous potassium hydroxide but dissolves gradually in boiling ethanolic potassium hydroxide. On acidification of the solution, extraction with ether and evaporation of the extract to dryness only a resin is obtained.

Octa-(n-propylsilsesquioxane), (n-C₃H₇Si)₈O₁₂

The above procedure is applied to 6.8 g (5.6 ml) of *n*-propyltrichlorosilane. The refluxing is continued for 48 hours. The crude product is recrystallized from 40 ml of acetone and then sublimed in vacuo (the order here is of little importance). Yield 1.6 g (44 %). For analysis the product was recrystallized once more from acetone and sublimed in vacuo.

$C_{24}H_{56}Si_8O_{12}$ (761.4) calc. C 37.86, H 7.41, M.W. 761;

found C 37.75, H 7.28, M.W. 760 (Rast).

The substance is very similar to the ethyl compound and exhibits polymorphism in the same way. An analytically pure sublimed sample melts at 216–218° (sealed

tube). If a sample recrystallized only once from acetone is melted by heating in a sealed tube to 220° and then allowed to cool in the melting point apparatus, it suddenly solidifies at about 170°. On repeated heating it melts almost completely at about 175°, solidifies again at about 205° and finally melts at 213–216°. Hence a modification melting at about 175° exists.

Octa-(n-butylsilsesquioxane), $(n-C_4H_9Si)_8O_{12}$

The above procedure is applied to 7.2 g (6.2 ml) of *n*-butyltrichlorosilane. The refluxing is continued for 96 hours (which may be insufficient to complete the reaction). The crude product is recrystallized from 10 ml of acetone and then distilled in vacuo. Yield 1.55–1.60 g (38–39 %). For analysis the product was recrystallized twice more from acetone and distilled in vacuo.

$C_{32}H_{72}Si_8O_{12}$ (873.6) calc. C 43.99, H 8.31, M.W. 874;
found C 44.03, H 8.16, M.W. 890 (Rast).

The compound forms rhombic plates very similar to those formed by the lower homologues. It melts at 73–76°.

Octa-(iso-propylsilsesquioxane), $[(CH_3)_2CHSi]_8O_{12}$

The above procedure is applied to 6.7 g (5.6 ml) of *iso*-propyltrichlorosilane. The refluxing is continued for 200 hours. The sublimation in vacuo of the crude product yields 2.5 g of crystals. These are recrystallized from 80 ml of acetone. Yield 0.63 g (17 %). The large amount of volatile impurities indicates incomplete reaction. For analysis the product was recrystallized twice more from acetone and sublimed in vacuo.

$C_{24}H_{56}Si_8O_{12}$ (761.4) calc. C 37.86, H 7.41, M.W. 761;
found C 37.66, H 7.29, M.W. 750 (Rast).

The substance is very similar to the ethyl compound. When placed in a sealed tube in a melting point apparatus preheated to 296° and adjusted to a rate of heating of 1° per minute, an analytically pure sublimed sample forms a clear melt at 300°. If allowed to cool in the melting point apparatus, it solidifies at 295°. On repeated heating, it melts at 295½°. If the alternate cooling and heating is continued in this way, only the higher melting point is observed, for in addition to the solid phase, which forms fairly rapidly at 295° on cooling, another one always starts to form slowly at 296½°. As is the case for the ethyl compound, the presence of this higher melting modification prevents the observation of the melting point 295½° of the lower melting modification. If the substance is first kept in a sealed tube at 295–300° for 2 hours, a clear melt forms at 297° on heating due to slight decomposition.

Octa-(phenylsilsesquioxane), $(C_6H_5Si)_8O_{12}$

The above procedure is applied to 8.0 g (6.0 ml) of phenyltrichlorosilane. The refluxing is continued for 12 hours. The crude product is refluxed for 30 minutes with 65 ml of acetone. The resulting suspension is left in the refrigerator for 24 hours. The precipitate is filtered off and washed with acetone. It weighs 0.56 g dry. It is recrystallized from 85 ml of pyridine, washed with acetone and dried in vacuo at

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100° for 1 hour. Yield 0.44 g (9 %). For analysis the product was recrystallized once more from pyridine, washed with acetone and dried as before.

$C_{48}H_{40}Si_8O_{12}$ (1034) calc. C 55.78, H 3.90;
found C 55.68, H 3.92.

The substance is almost insoluble in the usual solvents but is slightly soluble in pyridine and tetralin at their boiling points. It is usually obtained as a white microcrystalline powder, but fairly large crystals form from a pyridine solution saturated at the boiling point (115°) and left at 90° overnight. The characteristic rhombic shape of the alkyl compounds is easily recognized with the naked eye. The substance does not sublime at all when heated to 225° at 10 mm Hg for hours. In order to examine its stability against heat the compound was kept in a sealed capillary for 5 minutes at different temperatures in a melting point apparatus using a chromel-alumel thermocouple. The contents of the capillary were then observed under the microscope. At 460° very slight decomposition was found in this way, at 500° extensive decomposition, and at 510° only a yellowish transparent resin remained. Contrary to the alkyl compounds the phenyl compound dissolves rapidly in cold fuming nitric acid. If the solution is diluted with water, crystals of the usual rhombic shape are precipitated. Analysis and molecular weight agree with the formula $(O_2NC_6H_4Si)_8O_{12}$. The substance is fairly easily soluble in acetone in contrast to the unsubstituted phenyl compound.

Octa-(methylsilsesquioxane), (CH₃Si)₈O₁₂

To 180 ml of methanol in a 250 ml beaker are added with stirring first dropwise 5.7 g (4.4 ml) of methyltrichlorosilane and then rapidly 5.0 ml of conc. (aqueous) hydrochloric acid. The beaker is covered and left at room temperature for 10 days. The precipitate is collected, thoroughly washed with methanol and then with acetone and sucked completely dry. Now it weighs 1.6 g. From the acetone washings a small amount of a crystalline compound is obtained, which has not been studied further (*cf.* (3)). The main product is gradually heated in the sublimation apparatus to 225° at 10 mm Hg, kept at this temperature for 30 minutes, allowed to cool, powdered and finally heated to 225° in the same way for one additional hour. In all 1.0 g sublimes into the receiver. The sublimate is recrystallized from 50 ml of tetralin, washed with acetone and dried in vacuo at 110° for 1 hour. Yield 0.95 g (37 %). If 70 ml of the methanol is exchanged for methanolic hydrogen chloride, the reaction is complete in 1–2 days, but the yield is decreased to 29 %. Working at reflux temperature has a similar but stronger effect, and it is difficult to avoid severe bumping due to the bulky precipitate formed. For analysis the product was recrystallized once more from tetralin, washed with acetone and dried as before.

$C_8H_{24}Si_8O_{12}$ (537.0) calc. C 17.89, H 4.51;
found C 17.89, H 4.46.

The properties reported by Barry *et al.* (3) and by Sprung and Guenther (4, 5) have been completely confirmed. Though usually obtained as a microcrystalline white powder, it forms rather large crystals from a tetralin solution saturated at the boiling point (207°) and left at 180–190° overnight. The characteristic rhombic shape of the homologues is easily recognized with the naked eye. In order to examine its stability against heat the compound was kept in a sealed capillary for 5 minutes at 270° in a melting point apparatus. The capillary was then broken and kept at 225° and 10 mm Hg for 1 hour. A very small residue was obtained, proving slight decomposition. After treat-

ment at 310 and 350° in this way the residue amounted to about $\frac{1}{4}$ and $\frac{1}{2}$ respectively of the sample. The temperature of 540° mentioned in the text was measured with a chromel-alumel thermocouple.

Attempt to prepare octa-(tert-butylsilsesquioxane), $[(CH_3)_3CSi]_8O_{12}$

To 30 ml of methanol in a 100 ml flask was added in the usual way 1–2 g of impure *tert*-butyltrichlorosilane, 20 ml of methanolic hydrogen chloride and 1 ml of conc. (aqueous) hydrochloric acid. The solution was refluxed for 5 days and left in the refrigerator for 24 hours. The supernatant liquid was decanted from a minute amount of resin. This was dissolved in a small volume of acetone. The solution deposited a few crystals on cooling, which, however, did not suffice to fill a melting point capillary. Heating of the decanted liquid in a sealed tube to 150° for 26 hours was fruitless.

The infra-red spectra

The infra-red spectra were studied in the region 2–25 μ . A Perkin Elmer model 21 double-beam spectrophotometer equipped with sodium chloride, potassium bromide and caesium bromide prisms was used for the measurements. The substances were examined as solid pressed potassium bromide plates according to the method of Schiedt and Reinwein (10) and if possible in chloroform solution.

SUMMARY

A simple and reliable method to prepare compounds $(RSi)_8O_{12}$, where R is an alkyl or aryl group, has been worked out. The scope of the method has been studied. The yield ranges from 9 % of the phenyl compound to 44 % of the *n*-propyl compound. The properties of the products have been examined.

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The infra-red curves have been recorded by Mr. Stig Bergwall.

The analyses have been performed at the Analytical Department of this Institute.

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Laboratory of Organic Chemistry, Chemical Institute, University of Uppsala, April 1958.

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Studies on the metabolism of C¹⁴-labelled histamine in human plasma during pregnancy

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and H. WESTLING

Many *in vitro* studies have demonstrated an increased enzymatic histamine inactivation in human plasma during pregnancy. The activity of the enzyme during different stages of normal and pathological conditions of pregnancy and its correlation to various factors have been thoroughly investigated (for reviews see Ahlmark (1944), and Tabor (1954)).

The identity of the histaminolytic enzyme is still a matter of controversy. Zeller, Birkhäuser, Mislin and Wenk (1939) stated that the enzyme involved is diamine oxidase. This resulted from their finding that cadaverine and histamine were interchangeable as substrates and both amines were degraded under oxygen uptake. Werle and Effkemann (1940) came to the same conclusion on the basis of inhibitor experiments. Kapeller-Adler (1956) on the other hand has found that the ratio of the enzymic breakdown of cadaverine in relation to that of histamine varies considerably and concludes that the histaminolytic enzyme is not identical with diamine oxidase. Another possibility is suggested by the findings that methylation of histamine occurs to a considerable extent in man (Schayer and Cooper, 1956).

Identification of the metabolic products has not been made and would be of importance in establishing the nature of the enzyme responsible for histamine inactivation in plasma from pregnant women.

In the present communication is reported a search, by means of radioisotope methods, for histamine metabolites known to appear in the urine, as potential reaction products in pregnancy plasma. The absence of these metabolites being established and evidence for the presence of diamine oxidase being obtained by means of inhibitor experiments, an attempt was made to demonstrate the formation of imidazole acetaldehyde, this substance being the supposed primary reaction product of diamine oxidase action according to the conventional view (c. f. Tabor 1954).

Material and methods

Blood samples

Blood from women in the last weeks of pregnancy was withdrawn from the cubital vein, pooled and used for the experiments. Tricresol-free heparin was used

¹ During the tenure of a grant from the Swedish Natural Science Research Council.

in most experiments. The blood was centrifuged at $1000 \times g$ in the cold. The plasma was then incubated with labelled histamine at 37°C in air under constant shaking. Histamine concentrations from 0.2 to $1.7 \mu\text{g/ml}$ were used.

Assay for C^{14} histamine and its metabolites

Aliquots of the incubate were withdrawn at intervals for determination of histamine and the following metabolites: free and conjugated imidazole-4(5)-acetic acid (ImAA), 1-methylimidazole-4-acetic acid (methyl ImAA) and 1-methyl-4-(β -aminoethyl)imidazole (methylhistamine) with the isotope dilution technique developed by Schayer et al. (Schayer 1952, Schayer and Karjala 1956, Schayer and Cooper 1956, Rothschild and Schayer 1958). The method was described by Lindell and Schayer (1958). One microgram of C^{14} histamine, or its equivalent in metabolites, when counted under our standard conditions (with carrier added to give the equivalent of 206 mg of the picate, counted at infinite thickness in plates 1 inch in diameter, using a flow counter) gave 2040 c.p.m. All values in this paper are corrected for deviations (larger amounts of carrier or counting as pipsyl derivatives) from these standard conditions. The extraction with butanol described by Lindell and Schayer was found superfluous and has been omitted in some of these experiments.

Biological assay for histamine inactivation was performed as a complement to the isotope dilution technique in a few experiments. The description given by Wicksell (1949) was followed.

Aldehyde dehydrogenase

Racker (1955) has described a method for preparation of aldehyde dehydrogenase from beef liver. This method was adopted to obtain a crude enzyme preparation from rat liver, purified to the nucleic acid step. The activity was controlled by measuring the reduction of DPN, using acetaldehyde as a substrate.

Milk xanthine oxidase

A highly purified preparation at the stage immediate prior to crystallization (see Avis et al. 1956) was obtained from prof. F. Bergel (Royal Cancer Hospital, London) which is hereby gratefully acknowledged. The enzyme was dialyzed to eliminate the salicylate used as a stabilisator during storage. The enzyme activity was determined as described by Avis et al. (1955).

Substances

Histamine-(2-ring- ^{14}C)-dihydrochloride was purchased from Amersham, England. Inhibitors used were aminoguanidine in the form of the sulphate (Eastman Organic Chemicals, Rochester, U.S.A.) and semicarbazide hydrochloride, both dissolved in phosphate buffer pH 7.4.

Diphosphopyridine nucleotide (DPN) was purchased from Sigma Chemical Company.

Results

Preliminary experiments soon made clear that a satisfactory histamine destruction was obtained only if the incubations were prolonged considerably beyond

what was to be expected on account of information in the literature. Thus the highest rate of destruction found was $0.2 \mu\text{g/hr/ml}$ plasma and values down to $0.03 \mu\text{g/hr/ml}$ were noted. These results were confirmed by biological assay. On account of these findings subsequent incubations were carried on for up to 8 hours with intermittent withdrawal of samples for assays.

Analyses for metabolic products

The incubates on pooled plasma samples from three women in the last month of pregnancy was analyzed for histamine metabolites as described under methods.¹ Three different samples taken at four days' interval from one woman were incubated separately and analyzed for one or more metabolites.

It was found that less than 10 % of the destroyed histamine could be accounted for as known metabolites. Methylhistamine, methyl ImAA and conjugated ImAA were completely absent. ImAA was formed only in small amounts.

Effect of inhibitors

The effect of semicarbazide ($1 \cdot 10^{-2} M$) on the histamine destruction was tested in one experiment. Aminoguanidine ($1 \cdot 10^{-4} M$) was used as an inhibitor in four experiments. In all cases, within the experimental error, complete inhibition occurred. The course of experiments of this type is presented in table 1. The inhibition by aminoguanidine was confirmed by biological assay.

Table 1. Effect of aminoguanidine (AG) and semicarbazide (SC) on histamine destruction by human pregnancy plasma.

Each incubation flask contained plasma and C^{14} histamine in an initial concentration of $1.7 \mu\text{g/ml}$.

Flask no.	I	II	III
Inhibitor	none	AG	SC
Concentration of C^{14} histamine cpm/ml at zero time	3092	3152	2136
Concentration of C^{14} histamine cpm/ml after 8 hours	372	3136	1984

Enzymic oxidation of the reaction product

From the above inhibitor experiments it was concluded that the histaminolytic enzyme in pregnancy plasma behaved as diamine oxidase. The primary histamine metabolite therefore should be imidazole acetaldehyde² (see i.e. Tabor 1954). The fact that very little ImAA was formed was probably due to inability of the plasma to oxidize the formed imidazole acetaldehyde to ImAA.

To test this assumption experiments were carried out designed to bring about a further enzymic oxidation of the aldehyde.

¹ In this experiment the butanol extraction was omitted.

² In the early experiments a chloroform-extractable radioactive substance was encountered which was not methylhistamine. As none of the other known histamine metabolites is chloroform extractable, this substance may have been imidazole acetaldehyde.

Table 2. Analysis for histamine and imidazoleacetic acid (ImAA) after incubation of C¹⁴ histamine with pregnancy plasma and aldehyde dehydrogenase.

The flasks contained

- I. 8.5 ml plasma, 0.4 ml DPN in phosphate buffer (8 mg/ml), 1.0 ml 0.06 % versene.
- II. 8.5 ml plasma, 0.4 ml DPN, 1.0 ml aldehyde dehydrogenase in 0.06 % versene.
- III. 8.5 ml phosphate buffer, 0.4 ml DPN, 1.0 ml aldehyde dehydrogenase in 0.06 % versene.

Each flask contained C¹⁴ histamine in an initial concentration of 1.7 µg/ml.

Incubation time, hr	Per cent of radioactivity recovered as						Total recovery		
	Histamine ¹			ImAA					
	I	II	III	I	II	III	I	II	III
0	94	91	95	—	—	—	94	91	95
4	68	66	90	4	19	2	72	85	92
8	32	32	94	4	26	2	36	58	96

¹ The calculated maximal value is denoted as 100 %.

Table 3. Analysis for histamine and imidazoleacetic acid after incubation of C¹⁴ histamine with pregnancy plasma and xanthine oxidase.

All flasks contained 11.4 µg C¹⁴ histamine. Flasks nr I and II contained 8.5 ml plasma. In flask nr III phosphate buffer was substituted for plasma. Xanthine oxidase was added to flasks nr II and III every 15 minutes during the first 4 hours and thereafter on two more occasions. To flask nr I corresponding additions of buffer were made.

Incubation time, hr	Per cent of radioactivity recovered as						Total recovery		
	Histamine			ImAA					
	I	II	III	I	II	III	I	II	III
0	92	97	104	—	—	—	92	97	104
4	69	71	93	7	39	7	76	110	100
8	26	29	(78)	9	81	13	35	110	(91)

Aldehyde dehydrogenase

When aldehyde dehydrogenase and DPN were present during the incubation of plasma and histamine, a significant increase in ImAA formation was found without any accompanying increase in histamine destruction (see table 2). The histamine destruction encountered in the aldehyde dehydrogenase preparation itself was of the same magnitude as the experimental error of the method.

Xanthine oxidase

Addition of xanthine oxidase to the incubate resulted in a total conversion of the metabolized histamine to ImAA (table 3).

The histamine destruction in the flask containing only oxidase appeared to be high during the latter part of the experiment. Therefore the histaminolytic activity of the added enzyme was studied in a separate experiment with duplicate analyses. The histamine destruction was found to be within experimental errors. Hence it was concluded that the figure in table III (in brackets) was erroneous.

In the case of xanthine oxidase there is a quantitative conversion of inactivated histamine to ImAA. The rat liver dehydrogenase had not such a clear cut effect. This might be explained by its instability and decreasing activity during the incubation period (table II).

Discussion

A very remarkable feature of this investigation is the low histaminolytic activity encountered in pregnancy plasma (0.03–0.2 $\mu\text{g/ml/hr}$). The values reported here are well above Ahlmarks figures for non-pregnant women (average 0.005 $\mu\text{g/ml/hr}$; max. 0.015 $\mu\text{g/ml/hr}$; min. 0.002 $\mu\text{g/ml/hr}$) but very low compared with earlier investigations on pregnant women. Thus Ahlmark (1944) reports a mean value for the last five months of pregnancy on 3.0 $\mu\text{g/ml}$ plasma/hr and has never observed any value less than 1.6 $\mu\text{g/ml/hr}$ in any healthy pregnant woman after the 22nd week.

The reason for this discrepancy is not known. It has, however, not been possible to find any essential difference between the incubation method adopted here and that of Ahlmark. The question is under further investigation and it would be premature to offer any explanation.

Provided the histaminolytic activity analysed in this investigation is representative for the histamine destroying enzyme so conclusively demonstrated in pregnancy plasma by a great number of authors, the results reported here seem to be consistent with the assumption that the enzyme has the mode of action of diamine oxidase. Thus the histaminolytic activity was strongly inhibited by semicarbazide as previously reported by Werle and Effkemann, and by aminoguanidine, both substances being powerful diamine oxidase inhibitors (Zeller 1938, Schuler 1952). Furthermore the combined action of pregnancy plasma and aldehyde oxidase or xanthine oxidase leads to a conversion of histamine to imidazoleacetic acid, indicating that imidazole acetaldehyde is the primary degradation product of histamine in pregnancy plasma. This seems to be analogous to the observation by Tabor (1951) on purified diamine oxidase from pig kidney. He found that either aldehyde oxidase or xanthine oxidase causes a further oxygen uptake after the histamine oxidation is completed and, later (Tabor and Bauer, 1951) identified the end product as ImAA.

Apparently, methylation of histamine is not the cause of the histamine inactivation in pregnancy plasma under the present conditions.

SUMMARY

1. C^{14} histamine was incubated with plasma from pregnant women, and the rate of destruction followed. Less than 10% of the destroyed histamine could be accounted for in terms of known metabolites. 1-methylimidazole-4-acetic acid, 1-methyl-4 (β -aminoethyl) imidazole and conjugated imidazole-4 (5)-acetic acid were not formed. Imidazole-4 (5)-acetic acid was formed only in traces.

2. The histamine destruction in plasma from pregnant women was completely inhibited by semicarbazide and aminoguanidine, both potent diamine oxidase inhibitors.
3. The combined action of pregnancy plasma and xanthine oxidase or aldehyde dehydrogenase resulted in a conversion of histamine to imidazoleacetic acid.
4. It is suggested that the primary reaction product of the histamine metabolism in pregnancy plasma is imidazole acetaldehyde.

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Treatment of data from capillary measurements on non-Newtonian liquids

By ULV LOHMANDER

With 4 figures in the text

Introduction

This paper deals with the problem of calculating the viscosity as a function of the rate of shear (velocity gradient) from experimental data of a capillary viscometer. The gradient varies from zero at the center to a maximum value at the wall of the capillary. In Newtonian flow the viscosity is independent of the gradient while this is not so in non-Newtonian flow. Thus the main problem is to express, in measurable quantities, the viscosity or the gradient at a fixed distance from the center, e.g. at the wall of the capillary. The first suggestions to a solution of this problem were presented by Weissenberg (1) at the Science Research Meeting in Hamburg on September 21st 1928. A complete theory (2) was put forward after certain corrections had been made. The fundamental ideas of this theory will be briefly reported in the following.

Symbols used: P = applied pressure difference; L = capillary length; R = capillary radius; r = radius of any annulus within the capillary; v = velocity of flow at any annular distance r ; τ = shearing stress at any annular distance r ; τ_R = shearing stress at the wall of the capillary and Q = flow rate, volume per unit time.

The flow was assumed to be laminar and stationary and thus the velocity gradient was a function of the shearing stress

$$-\frac{\partial v}{\partial r} = f(\tau) \quad (1)$$

The flow rate was

$$Q = 2\pi \int_0^R v r dr = 2\pi \left(\left[v \frac{r^2}{2} \right]_0^R - \int_0^R \frac{r^2}{2} \frac{\partial v}{\partial r} dr \right) \quad (2)$$

The first term of the right membrum would be zero if there were no slippage at the wall.

Noting $\tau = \frac{rP}{2L}$ and introducing

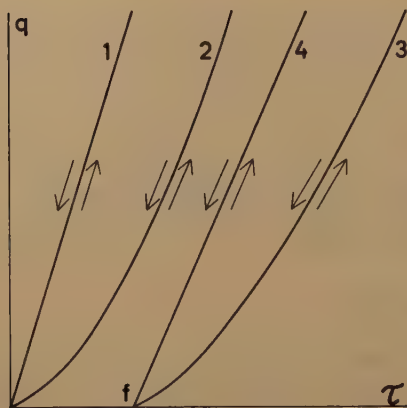


Fig. 1. Rate of shear (q) vs. shear stress (τ).
1: Newtonian, 2: pseudoplastic, 3: plastic,
4: Bingham flow.

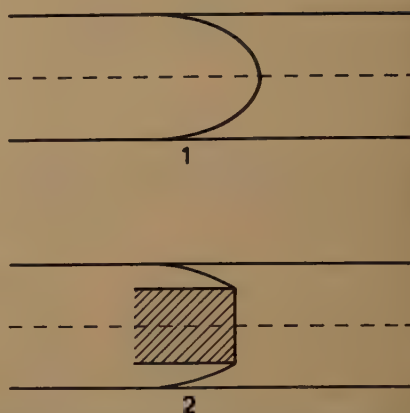


Fig. 2. Variation of flow velocity across a capillary. 1: Newtonian, 2: plastic flow.

$$F(\tau) = \frac{1}{\tau^3} \int_0^\tau \frac{\tau^2}{2} f(\tau) d\tau \quad (3)$$

$$\text{gave by comparison with equation (2): } F(\tau_R) = \frac{Q}{2\pi R^3} \quad (4)$$

Equation (3) gave by derivation

$$f(\tau) = 6F(\tau) + 2\tau \frac{dF(\tau)}{d\tau} \quad (5)$$

i.e. at the wall of the capillary

$$-\left(\frac{\partial v}{\partial r}\right)_{r=R} = 6F(\tau_R) + 2\tau_R \frac{dF(\tau_R)}{d\tau_R} \quad (6)$$

Equation (6) gave the desired correlation between the velocity gradient and the shearing stress *at the wall of the capillary*.

During the last three decades several authors (5-10) have treated the problem but nothing fundamentally new has come out since the work reported by Weissenberg and collaborators (1-4). Nevertheless, statements such as "——— we evolved the following formula which, so far as we are aware, makes it for the first time possible to calculate the actual viscosity ———" (5) and "A powerful new scheme is presented for analyzing the results of capillary flow measurements on non-Newtonian liquids" (8) have been reported in literature.

To avoid any confusion regarding the meaning of the names assigned to specific flow anomalies, they are defined here in the sense in which they will be used in the following. Fig. 1 shows a rheogram where the rate of shear (q) is plotted against the shearing stress (τ) for different types of fluid flow. For a *Newtonian* liquid the curve becomes a straight line passing through the origin and the viscos-

ity $\left(\eta = \frac{\tau}{q}\right)$ is independent of the rate of shear (q). With *pseudoplastic* materials the relation between shear and stress is non-linear (Fig. 1:2). Pseudoplasticity is characterized by the lack of a real yield stress (see below), the lack of influence of time and the property of instantaneous reversion. In a *plastic* system, force can be applied up to a critical point without causing any flow. The force per unit area required to bring about the flow is called the yield stress (f). Above this minimum force, the curve (Fig. 1:3) looks similar to that representing pseudoplastic flow (Fig. 1:2). Plasticity is characterized by the existence of a real yield stress and the lack of influence of time. It should be pointed out here that the definition of plastic materials given above is more general than in Bingham's sense. *Bingham bodies* are characterized by a definite yield point, viscosity being constant after the flow starts (Fig. 1:4).

Instead of a parabolic curve for capillary flow velocities a different form will be found, as shown in Fig. 2:2 for a plastic material. The central part of the material in the tube moves as a unit, since the stress is insufficient to overcome the yield value; hence the name 'plug-flow' for extreme cases of this behaviour. It should be observed that no part of the velocity curve in Fig. 2:2 has to be parabolic.

Previous authors (1-10) have mainly discussed the problems of determining the viscosity from capillary measurements for pseudoplastic and Bingham materials. In section (1) of the present work a complete treatment is given for plastic flow while in section (2) apparent viscosities are discussed.

(1) Viscosity — rate of shear relation in the case of plastic flow

The connection between viscosity and shear rate is immediately obtained from the differential equation appropriate to capillary flow. In the following the deduction of this differential equation is made applicable to plastic liquids.

The following symbols are used: η = viscosity at any annular distance r ; f = yield stress; P , L , R , r , v and Q have the same meaning as in the introduction.

The flow is assumed to be stationary and laminar. The element chosen (Fig. 3) is a cylindrical envelope (radius r , thickness dr , length L) situated concentrically in the capillary outside the range of plug flow. The applied pressure difference acts on the upper surface $2\pi r dr$ and the frictional forces act on the two cylindrical areas of the envelope $2\pi r L$ and $2\pi (r + dr) L$ respectively. Hence

$$P 2\pi r dr - \eta 2\pi r L \frac{dv}{dr} + f 2\pi r L = f 2\pi (r + dr) L - (\eta + d\eta) 2\pi (r + dr) L \left[\frac{dv}{dr} + d \left(\frac{dv}{dr} \right) \right] \quad (7)$$

If the terms of higher orders are neglected, one obtains

$$-\frac{Pr}{L} + f = \eta \frac{dv}{dr} + \eta r \frac{d^2v}{dr^2} + \eta \frac{d\eta}{dr} \frac{dv}{dr} \quad (8)$$

$$\text{or} \quad -\frac{Pr}{L} + f = \frac{d}{dr} \left(\eta r \frac{dv}{dr} \right) \quad (9)$$



Fig. 3. Cylindrical envelope.

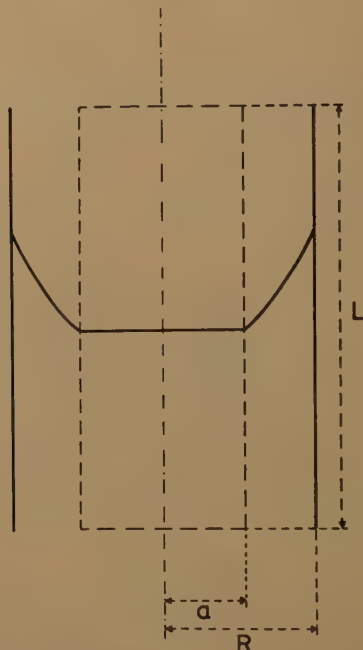


Fig. 4. Capillary with velocity profile for plastic flow.

Equation (9) is the differential equation representing the general case of plastic flow.

Fig. 4 shows a longitudinal cut through the capillary with the velocity profile for plastic flow (continuous line). The range of plug flow is limited by $r = a$. Integrating equation (9) between the limits a and R gives

$$\int_a^R \left(-\frac{Pr}{L} + f \right) dr = \int_{r=a}^{r=R} d \left(\eta r \frac{dv}{dr} \right) \quad (10)$$

$$\text{or} \quad -\frac{PR^2}{2L} + \frac{Pa^2}{2L} + fR - fa = \left(\eta r \frac{dv}{dr} \right)_{r=R} - \left(\eta r \frac{dv}{dr} \right)_{r=a} \quad (11)$$

The central part of the material in the capillary moves as a unit (marked with lines of short dashes in Fig. 4). The forces acting on the unit are the force of driving pressure and the frictional forces. Hence

$$\pi a^2 P = f 2\pi a L - \left(\eta \frac{dv}{dr} 2\pi r L \right)_{r=a} \quad (12)$$

$$\text{or} \quad \frac{Pa^2}{2L} - fa = - \left(\eta r \frac{dv}{dr} \right)_{r=a} \quad (13)$$

Combining equations (11)–(13):

$$-\frac{P R^2}{2 L} + f R = \left(\eta r \frac{d v}{d r} \right)_{r=R} \quad (14)$$

or

$$-\frac{P R}{2 L} + f = \left(\eta \frac{d v}{d r} \right)_{r=R} \quad (15)$$

Introducing:

$$q = - \left(\frac{d v}{d r} \right)_{r=R}$$

$$\eta = (\eta)_{r=R}$$

$$\eta' = \frac{P R}{2 L q} \quad (16)$$

one obtains

$$\eta = \eta' - \frac{f}{q} \quad (17)$$

Equation (17) gives the desired connection between η and q (i.e. viscosity and velocity gradient *at the wall of the capillary*) in the general case of plastic flow. For pseudoplastic materials $f=0$ and therefore in this case η' represents the viscosity.

Earlier Weissenberg and coworkers (1–4) derived an expression, viz. equation (6), for the velocity gradient at the wall of the capillary. This equation can be transformed to

$$q = \frac{1}{\pi R^3} \left(3 Q + P \frac{d Q}{d P} \right) \quad (18)$$

As is easily seen from the deduction, equation (18) is valid even in case of plastic flow.

In order to get the viscosity expressed in data from common measurements the following symbols are introduced: V = volume of bulb; Δt = effluent time; η^* = apparent viscosity and q^* = apparent velocity gradient at the wall of the capillary

$$\text{where} \quad \eta^* = \frac{\pi R^4 P \Delta t}{8 V L} \quad (\text{Poiseuille's formula}) \quad (19)$$

$$q^* = \frac{P R}{2 \eta^* L} = \frac{4 V}{\pi R^3 \Delta t} \quad (20)$$

Noting $Q = \frac{V}{\Delta t}$ and introducing

$$F(P) = - \frac{d \ln \Delta t}{d \ln P} \quad (21)$$

one gets from equations (16)–(20)

$$q = q^* \frac{3 + F(P)}{4} \quad (22)$$

and

$$\eta = \eta^* \frac{4}{3 + F(P)} - \frac{f}{q} \quad (23)$$

The only term unknown in the right membrum of equation (23) is f which can be easily determined if the pressure $P_{\min}$ necessary to start any flow is known. Then

$$f = \frac{P_{\min} R}{2 L} \quad (24)$$

(2) Apparent viscosities from capillary measurements. Some comments

In this section data obtained from measurements with a special kind of viscometer are discussed. The viscometer is assumed to consist of cylindrical tubes connected by a capillary (11). The "bulb volume" therefore becomes

$$V = \frac{1}{\varrho g} \left(-\frac{\Delta P}{2} \right) \pi b^2 \quad (25)$$

where ϱ = density of the liquid;

g = gravitation constant;

ΔP = change of driving pressure in the time Δt ;

b = radius of cylindrical tubes.

If ΔP is small compared to P , equations (19) and (25) give

$$\eta^* = -\frac{R^4 \varrho g}{4 b^2 L} \cdot \frac{P \Delta t}{\Delta P} = -K P \frac{dt}{dP} \quad (26)$$

where K = a positive constant. If the driving pressure at time zero is P_0 , integrating gives

$$\int_{P_0}^P \frac{dP}{P} = -K \int_0^t \frac{1}{\eta^*} dt = -\frac{K}{\eta^*} \int_0^t [1 + f_1(t)] dt \quad (27)$$

$$\ln \frac{P_0}{P} = \frac{K}{\eta^*} [t + f_2(t)] \quad (28)$$

Introducing

$$\eta^{**} = K \frac{t}{\ln \frac{P_0}{P}} \quad (29)$$

one obtains

$$\eta^* = \eta^{**} + K \frac{f_2(t)}{\ln \frac{P_0}{P}} \quad (30)$$

For a *Newtonian* liquid η^* is a constant. Thus in this case $f_1(t) = f_2(t) = 0$ and so $\eta^* = \eta^{**}$. It may be noted that to consider η^{**} to be the true viscosity of a non-Newtonian liquid is incorrect. Golub (12) has, however, compared η^* and η^{**} with each other disregarding the fact that these quantities are not identical.

If t is known as a function of P , η^{**} is easily calculated from equation (29) and then calculation of η^* from equation (26) would seem quite simple too. Large errors are, however, introduced in graphic determinations of $\frac{dt}{dP}$ and from equation (26) it is obvious that these errors have large effect upon η^* . To avoid this source of error a transformation is made, viz. introducing

$$H(P) = \frac{t}{\ln \frac{P_0}{P}} \quad (31)$$

Hence
$$\frac{dt}{dP} = H(P) \left(-\frac{1}{P} \right) + H'(P) \ln \frac{P_0}{P} \quad (32)$$

Multiplying equation (32) by $-KP$ and identifying from equations (26) and (29) one gets

$$\eta^* = \eta^{**} - KP H'(P) \ln \frac{P_0}{P} = \eta^{**} + \Delta \eta^{**} \quad (33)$$

In order to calculate η^* from equation (33) the derivate $H'(P)$ has to be known and this can be determined graphically. An error in $H'(P)$ has only a small effect on η^* since $|\Delta \eta^{**}| \ll \eta^{**}$.

It is obvious that for viscometers with bulbs, the only method to find η^* is to use Poiseuille's formula viz. equation (19). Even for viscometers consisting of cylindrical tubes connected by a capillary, equation (19) is valid if the time is taken differentially as for bulb viscometers. For very small driving pressures, however, it is for practical reasons advantageous to read the position of the meniscus continuously and in that case equation (33) should be used to determine η^* .

SUMMARY

A complete deduction is given for the viscosity — rate of shear relation in the case of plastic flow. Apparent viscosities are discussed and a method is presented for the treatment of data obtained from measurements with a viscometer consisting of cylindrical tubes connected by a capillary.

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